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Current Review

THE MODE OF ACTION AND THE CLINICAL APPLICATION OF CARBONIC ANHYDRASE INHIBITOR (ACETAZOLEAMIDE) IN OPHTHALMOLOGY

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It is now three years since therapeutic carbonic anhydrase inhibition was introduced into ophthalmology.[1-6a] It was immediately apparent in 1953 that a new and potent agent for the medical treatment of glaucoma was at hand. The accumulated experiences of these years have fully confirmed early expectations and have served to define the potentialities and limitations of this form of therapy. This development has, in fact, been a tremendous stimulus to basic investigation into aqueous dynamics and for this reason, too, we should be grateful. Some 70 papers have thus far appeared in the world literature attesting the importance of acetazoleamide and one may predict a manifold increase in the next few years.

By far the most extensive laboratory and clinical investigations have been carried out by Becker and his associates. Frequent reference will be made to his work in this review.

GENERAL BACKGROUND OF ACETAZOLEAMIDE THERAPY

The enzyme carbonic anhydrase is found in red blood cells, kidney, stomach, pancreas, brain and ocular tissues. It plays an important role in the reversible hydration of carbon dioxide to form carbonic acid: $H_2O + CO_2 \rightleftharpoons H_2CO_3$. This reaction is markedly accelerated in the presence of the enzyme but will occur spontaneously at a slow but appreciable rate in its absence. In the epithelium of the renal tubule the dissociation of $H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$ makes H^+ available to exchange with Na^+ from the filtrate in the tubule lumen, thus conserving base. When renal carbonic anhydrase is blocked with acetazoleamide there is interference with the production of hydrogen and bicarbonate ions and a decrease in the conservation of base so that an alkaline urine is excreted containing bicarbonate, Na^+, K^+, and other ions. This diuresis is utilized in treatment of cardiac edema, premenstrual tension, etc.

THE BACKGROUND OF ACETAZOLEAMIDE THERAPY IN OPHTHALMOLOGY

Carbonic anhydrase is important wherever a secretion rich in bicarbonate is elaborated. In the eye, it has been found in the ciliary processes and iris, lens and retina. Following the demonstration by Kinsey of the high concentration of bi-

carbonate in the aqueous and because of Friedenwald's theory of enzymatic secretion of hydroxyl ions in the ciliary epithelium it was apparent to many workers that carbonic anhydrase might be implicated in this process. Thus inhibition of this enzyme might alter aqueous formation and, hence, intraocular pressure. It is now well known that acetazoleamide does inhibit the carbonic anhydrase present in the ciliary body[7] and that it does affect the intraocular pressure. This action is independent of renal function.

Although it seemed unquestionable in the early days that the mechanism of action was to impede the secretion of bicarbonate into the aqueous and that the locale of action was the ciliary body, subsequent conflicting studies have confused the picture and created the impression that the medication was right but for the wrong reasons. Green *et al.*[7, 8] have reported that acetazoleamide produced no significant fall of either aqueous or plasma bicarbonate after subconjunctival or intravenous injection in the rabbit, nor did the intraocular pressure fall. Harris[8] and Langham[9] each reported a concomitant but equal fall of aqueous and plasma bicarbonate indicating a systemic rather than ocular basis of action. On the other hand, Becker[13] showed that a significant fall of aqueous bicarbonate did occur with little change in plasma bicarbonate. This has been confirmed by Kinsey *et al.*[14] and in part by Lee[10]. Urrets-Zavalia[34] reported a decrease in aqueous osmolarity in dogs presumably based on a diminution of electrolytes.

All workers agree that local applications of acetazoleamide were without effect on pressure[11–13] and electrolyte concentrations, even though inhibition of carbonic anhydrase occurred in the ciliary epithelium. Significantly, intracarotid injection also was ineffective[11]. This makes it difficult to define conclusively the locus and mode of action of the drug despite the strong probability that it acts on the ciliary body carbonic anhydrase.

Tonography has proved an excellent tool for analysis of the effects of acetazoleamide upon aqueous dynamics. It is clear that no change in facility of outflow is produced by acetazoleamide in short term therapy[15]. The drug lowers intraocular pressure in man and animals by decreasing the rate of flow of aqueous. This concept is supported by the observed delay in fluorescein appearance time and changes in bicarbonate and ascorbate ratios[16, 17]. Nevertheless, one of the commonest experiences in clinical practice and in laboratory studies is the finding of unresponsive subjects who fail to exhibit the expected lowering of pressure after the use of acetazoleamide. Of particular significance is the almost universal experience that many patients can be controlled for a short time, after which the pressure rises again. Tonography has provided an answer to some of the confusing reports on responsiveness of man and animals. When non-responsive rabbits were evaluated by tonography it became apparent that although inhibition of flow occurred it was masked by a compensatory decrease in facility of outflow. Thus little or no change of intraocular pressure was observed. This demonstrated the need to evaluate the pharmacologic effectiveness of acetazoleamide in terms of inhibition of flow rather than in terms of intraocular pressure. How the animals altered their facility of outflow is quite unknown but the effect

could be blocked by fluorohydrocortisone[16]. This blockage does not seem effective in man.

It is important to emphasize that some resistance to the effect of glaucoma patients stems from improper timing of dosage. The recovery of intraocular pressure after a single dose of acetazoleamide is partly by decrease in facility of outflow 6 to 24 hours later. This occurs while secretion is still inhibited. A second dose may now encounter a non-responsive mechanism. Of course, if a sufficiently long time elapses between doses there will be a return of the original effect but this presupposes an uncontrolled interim. For this reason 24-hour maintenance levels are deemed essential. Tachyphylaxis, i.e., true tolerance, occurs infrequently. Here there is a loss of pharmacologic effect after a period of effectiveness and both outflow and inflow are unaffected by administration of the drug.

Friedenwald postulated the main site of carbonic anhydrase activity to be in the stroma of the ciliary body.[17] He felt that acidosis potentiated the effects of acetazoleamide at that site. Ammonium chloride in doses of 1 to 2 gm. three times daily occasionally may overcome refractoriness, presumably on this basis.

It has been determined that maximum inhibition of carbonic anhydrase leads to about 60 per cent inhibition of flow. Hence the uncatalyzed reaction can still permit about a 40 per cent rate of flow. In other words approximately one third of the rate of secretion is *independent* of carbonic anhydrase. This is of basic importance since it indicates that there is a limit to inhibition of flow by carbonic anhydrase no matter how large the dose. Furthermore, the residual 40 per cent of uncatalyzed flow may still permit intraocular pressures to remain at levels far above the normal. The residual flow is probably a safety factor preventing ocular toxicity, and is sufficient to adequately convey nutriments and remove wastes.[16] Complete suppression of flow, as produced by surgery or disease, results in cataracts and other severe disturbances.

Acetazoleamide has little effect upon an eye in which the rate of secretion is already low—less than 1 cu. mm./minute.[18] Such spontaneously decreased rates of flow are encountered in some animals and in man in low tension glaucoma. Decreased flow may be responsible for some types of refractoriness.

Increasing impairment of facility of outflow is another cause for the failure of response in protracted therapy. This decreased outflow may result from progression of the disease or may conceivably be a consequence of acetazoleamide therapy. However induced, it can limit the hypotensive action of the drug and nullify its benefits. Tonographic studies, nevertheless, will usually reveal that inhibition of secretion is present.

One of the earliest and most important observations made on the use of acetazoleamide was its potent synergism with miotics.[2, 3] It is now axiomatic that acetazoleamide should not be given solely but should always be an adjunct to miotics. By itself, acetazoleamide is inadequate to control most glaucomas. It is clear that it controls only the entry and not the exit of fluid. Miotics, on the other hand, have been shown to improve the outflow and do not affect

the inflow of fluid. The combination provides the greater effectiveness of improved outflow and decreased inflow. Becker feels that normalization of outflow is necessary to prevent deterioration of field whereas Grant feels that so long as tension is normalized it makes no difference whether it is brought about by one or the other method.[19]

Because the fundamental disturbance in most glaucomas is an impairment of outflow it would appear more physiologic to normalize pressure by removing this obstruction rather than by decreasing the inflow. Since miotics act to improve the outflow they retain a primacy in therapy which cannot be supplanted. Suppression of inflow can only be an adjunct to be employed where miotics alone are unable to effect normalization of intraocular pressure and, possibly, facility of outflow. The undesirable side effects of acetazoleamide therapy, to be discussed later, lend weight to this conclusion. It is thus still true that miotics remain the basic treatment for glaucoma.

DOSAGE FORMS AND SCHEDULES

Acetazoleamide (Diamox) is supplied in the form of 250 mg. scored tablets; 50 mg. scored tablets; ampoules containing 500 mg. to be made up in 10 cc. distilled water for intravenous or intramuscular injection; (250 mg. in 5 cc. distilled water); 125 and 250 mg. formalinized gel, delayed action capsules. There is considerable variation in dosage recommended in the literature. Generally 1 gm. of the drug is given daily in divided doses (250 mg. every 6 hours). This supplies a 24-hour maintenance level. The importance of a constant, maintenance level for the control of glaucoma deserves re-emphasis. Failure to attain this may cause refractoriness or intermittent control only. Damaging tension spikes may occur and not be observed by the ophthalmologist in such patients. It may be that some patients can be made normotensive with intermittent therapy or even an occasional dose but this, in general, provides a most uncertain and probably illusory control. In primary glaucoma and wherever indicated, miotic therapy must not be stopped. Although 1 gm. a day of acetazoleamide is most generally employed for adults there are many patients who can be controlled on smaller dosage (5 to 10 mg./kg.). When using such a potent agent it is wise to administer the smallest effective dose rather than the largest. In my experience 125 mg. every 6 hours is frequently satisfactory. Each patient should be carefully observed to establish the minimal effective dosage and just as carefully followed. In order to avoid the inconvenience of frequent administration the delayed action type of capsule may be given. This requires about 6 hours to dissolve before releasing the drug. Thus if a tablet of regular and a capsule of slow release type are given together the slow one becomes effective in about 6 hours, just as the regular one is being excreted, effectively providing 12-hour control. By giving 1 of each at 12-hour intervals a 24-hour level is attained. The delayed action capsules are sometimes not assimilated but pass right on through the GI tract thus contributing to nonresponsiveness. In some instances they have accumulated, unabsorbed in the gut. It is therefore wise to utilize the regular tablets at the start. One may switch over with care later. The coating has recently been modified to permit better absorption.

For the vomiting patient with acute glaucoma unable to tolerate oral tablets the parenteral route is rapidly effective and safe. As much as 250 to 500 mg. in 5 to 10 cc. distilled water may be injected intravenously.

For infants a total of 100 to 200 mg. a day in divided dosage is effective. The tablets are crushed and mixed in cereal or formula given every 6 hours. For children an intermediate range of dosage is used (50 to 125 mg. every 6 hours).

THE THERAPY OF THE GLAUCOMAS AND OTHER OPHTHALMIC USES OF ACETAZOLEAMIDE

The ophthalmic uses of acetazoleamide are as follows: (1) Glaucomas of all types—short and long term therapy. (2) Preoperative—to lessen surgical complications of the hard eye. (3) Diagnostic—to permit gonioscopy, ophthalmoscopy, evaluation of vision and field; dilated pupil. (4) Temporizing—in poor risks. (5) Corneal edema clearance—(A) glaucoma; (B) corneal dystrophies. (6) Flat chamber—after cataract and glaucoma surgery. (7) Protruding corneal transplants.

An impressive world wide literature has accumulated on the subject of glaucoma control through carbonic anhydrase inhibition. All attest to the efficacy of acetazoleamide plus miotics in short term therapy of glaucoma.[2, 3, 20, 21, 31] There is apparently no form of glaucoma in which some lowering of intraocular pressure has not been obtained. In many the hypotensive effect is profound. Numerous cases uncontrolled on miotics and surgery have responded dramatically on the addition of acetazoleamide. Nevertheless it is everyone's experience that there are cases which exhibit no decrease in pressure or a decrease inadequate to normalize pressure and prevent the progression of ocular damage.

There is general agreement that attacks of acute closed angle glaucoma often respond dramatically. Following an initial 500 mg. orally and 250 mg. every 6 hours the pressure begins to fall within several hours but may not reach maximum depression for 6 to 18 hours. The usual intensive miotic therapy must not be omitted. Once the pressure is normalized the drug may be discontinued and the patient maintained on miotics until surgery can be performed on the noncongested eye. Although many acute attacks are overcome with miotics alone it appears wise to use both agents together thus favoring the most rapid and effective pressure drop. If the patient is vomiting and unable to tolerate oral medication, intramuscular or intravenous injection is indicated. The response is quicker, more effective, and no untoward reactions have been reported. A dose of 250 mg. of the parenteral preparation in 5 cc. of distilled water or 500 mg. in 10 cc. of distilled water should be given slowly. The smaller dose may be repeated in several hours. Once the severity of the attack is modified, the oral medication may be substituted. The use of chlorpromazine to control nausea and vomiting may permit early oral administration.[20]

It does not appear wise to use the drug prophylactically since it is unlikely that subsequent attacks can be completely prevented and the problems of long term medication enter the picture. Furthermore, repeated congestive episodes facilitate formation of goniosynechiae and may result in the development of a chronic closed angle glaucoma. It is a fact that many patients prefer the con-

tinued use of acetazoleamide to remedial surgery which is still the only effective answer to the problem of acute closed angle glaucoma. This is a development which may be expected to increase in significance with time. It is important to stress that acetazoleamide is not a substitute for surgery in closed angle glaucomas.

Acute secondary attacks have long been among the most difficult of ophthalmic problems. The juggling of mydriatics and miotics in uveitic hypertension is fraught with dangers and often proves unavailing. With the use of acetazoleamide the tension can be lowered to the point where mydriatics may safely be used along with indicated steroids. After this there may be no further need for acetazoleamide and one is concerned solely with treating the underlying disease. This has proved to be a most gratifying and important application. It has been suggested that serious potassium loss may be engendered by combined acetazoleamide and steroids[5] but this does not appear to be a significant problem. The possibly favorable influence of acetazoleamide *per se* on uveitis in rabbits has been reported.[33]

Chronic closed angle glaucoma is associated with a higher incidence of refractoriness. In this, as in the acute types, congestive episodes may be controlled by the drug and patients have aborted attacks by taking one or two tablets when premonitory symptoms developed.

Secondary glaucomas of diverse etiology, uncontrolled by standard medication, may often be normalized by the addition of acetazoleamide. The maintenance of control varies with the etiology and progression of the underlying disease. The favorable response of the uveitis group (including glaucomatocyclitic crisis) has already been alluded to.

The hypotensive action of acetazoleamide enables the surgeon to operate on a soft eye with a lowered incidence of operative complications. It facilitates the extraction of an intumescent lens in the presence of elevated pressure, the handling of traumatic glaucoma, dislocated lenses and aphakic glaucoma.

The treatment of hyphema accompanied by hypertension is of interest because the pressure lowering effect of acetazoleamide may induce further bleeding. The drug seems to prolong absorption of blood from the anterior chamber favoring the development of extensive synechiae and obstructive membranes.[22] Irrigation of the anterior chamber at an appropriate time appears indicated.

Congenital glaucomas can be treated with frequent, small doses of acetazoleamide. Tension can be normalized long enough to carry out careful diagnostic examination and for longer periods to permit surgery under more favorable conditions. One type of infantile glaucoma which deserves special mention is the Sturge-Weber or nevus flammeus group. Tonography has revealed hypersecretion patterns in several cases. A six-month-old child had buphthalmos on the side of an extensive nevus flammeus involving the face, lids, forehead and extremities. Tonometry under general anesthesia revealed elevated pressures in both eyes on many occasions. Tonographic study showed normal to low normal facilities of outflow in both eyes and increased rates of secretion. Three surgical procedures were performed on the buphthalmic eye which converted it into the

typical outflow block pattern and failed to control the pressure over a period of 18 months. Acetazoleamide was prescribed along with usual miotics and the pressure of both eyes returned to normal limits over a 24-month period of observation. The favorable response of such an unfavorable condition is important, since the outlook is generally so poor. The necessity for long term therapy, however, raises serious problems.

The least favorable responses to acetazoleamide are reported in hemorrhagic glaucoma due to diabetic rubeosis or central vein thrombosis. The reason for this is not clear. Extensive peripheral anterior synechiae, however caused, limit its hypotensive effect.

Long Term Therapy of Glaucoma. The problem of medical management of simple glaucoma looms large in ophthalmic therapeutics. It was hoped that acetazoleamide would prove an efficient and safe agent for the chronic medication of these patients. There is now a general feeling that this wish will not be realized. The reasons are chiefly two: one, that side reactions are too frequent and too unpleasant; two, the difficulty in maintaining effective tension control over long periods of time.

The long term studies that have been published show about 50 per cent success in maintaining therapeutic control in all types of glaucoma.[23, 24, 31, 32] Chronic narrow angle showed the least favorable results (only 20 per cent) and open angle glaucoma the best (60 per cent). Secondary types had a 50 per cent success. The failures appeared due about equally to side effects and inadequate control.

The reasons for inadequate control have been previously discussed. The factor of a progressive decrease in facility of outflow requires further study before conclusions may be drawn. In the series of Kupfer *el al.*,[24] the average facility of outflow was not decreased.

A relatively high incidence of failure is produced by side effects of the drug which make it impossible for many patients to continue therapy for long periods. In private practice the number of failures for this cause is far greater than one would gather from data on clinic patients. It has been the experience of my colleagues and myself that few patients tolerate round the clock medication for periods of months—this is the chief reason for failure in our hands. It is also my experience that the degree of control reported above is somewhat more favorable than I have encountered. I see many patients whose tension cannot be normalized for long periods with therapeutic doses. This was also reported by Leopold and Carmichael[31] who cited the development of resistance in 23 cases; loss of control was responsible for 36 out of 44 failures. Supplementary ammonium chloride has not been especially helpful. For these reasons we reserve the medication for short term therapy almost entirely. Chronic medication is used only where other treatment has failed and surgery is contraindicated or refused. This policy has been reported by others.[31, 32]

Flat Chamber After Cataract and Glaucoma Surgery. Thorpe has reported the favorable influence of acetazoleamide in restoring flat anterior chambers with choroidal separation after surgery. He ascribed this to dehydration and change

in blood electrolyte balance causing a reduction of choroidal effusion and possible shrinkage of vitreous. Friedenwald felt that the decrease in flow might facilitate fibroblastic repair of a leaking wound. Several reports[26, 27] have confirmed this restoration. One stated that 40 out of 45 flat chambers were so restored.[27] Others have been unimpressed.[32] My experience in this has been inconsistent—some chambers have reformed after acetazoleamide while many others have not. In view of the spontaneous reformation of chambers which so often occurs, further controlled studies should be carried out.

Corneal Edema. It has been observed that corneal edema accompanying elevated pressure will clear on securing a fall in pressure through acetazoleamide. Occasional edemas without elevated pressure may also be cleared. The mechanism in these is obscure but may depend on systemic effects of the drug. No carbonic anhydrase has been found in the cornea. A particularly interesting patient I observed developed an acute keratoconus with a large bulla. With a 500-mg. dose the bulla flattened out in an hour. The possibility that keratoconus stems from intraocular pressure too great for its tissue resistance suggests the possible application of acetazoleamide in this condition.

Stocker has reported the ability of acetazoleamide to clear corneal edema and improve vision in the corneal dystrophies, including the Fuchs' endothelial-epithelial dystrophy using very small doses at infrequent intervals. My experiences with a number of the latter type have been uniformly negative.

No benefit has been obtained in central serous retinopathy.

Corneal transplants do well with the lowered pressure induced by acetazoleamide. It is also said to be particularly useful in reducing bulging of a transplant.

Acetazoleamide is an important aid in permitting more detailed diagnostic study in congestive glaucoma. With lower pressure and a clear cornea careful fundus examination and gonioscopy can be carried out. Visual fields can also be taken. The ability to dilate the pupil is most important since this may be dangerous in closed angle glaucomas and is often neglected in all types of glaucomas. The tension may still rise but it provides a definite safety factor.

Acetazoleamide plays an additional role in temporizing in poor risk patents who cannot or will not undergo surgery. Other uses will undoubtedly appear.

SYSTEMIC TOXICITY OF ACETAZOLEAMIDE

The profound influence of this potent agent upon acid-base buffering mechanisms throughout the body makes it inevitable that systemic side reactions should arise. The large safety factor in the quantitative interaction of carbonic anhydrase and its inhibitor preserves the patient from serious derangements of vital functions with therapeutic doses. This does not preclude the possibility, however, that such derangements may occur. The sulfonamide nature of acetazoleamide also leads to the production of toxic reactions characteristic of sulfonamides; thus we have seen skin eruptions and granulocytopenia; thrombocytopenia, agranulocytosis, renal lesions, calcinosis and renal colic have been

reported. Hematuria, casts and albumen appeared in the urine of several of our patients without antecedent renal disease. These cleared on cessation of acetazoleamide therapy. Formation of renal stones has been noted in several clinics.

The almost universal side effect developed by patients on acetazoleamide therapy are paresthesias of the face, hands and feet. These occur in at least 70 to 80 per cent of patients[23, 31] and occasionally require cessation of treatment.

Nausea and anorexia are also common (50 per cent) and not infrequently require stopping treatment. Fatigue is occasionally experienced. Other reactions cited are hearing loss and vertigo. Although these effects are reversible when the drug is stopped they constitute a serious impediment to its prolonged use. Blood and urine studies should be obtained at intervals.

OCULAR TOXICITY OF ACETAZOLEAMIDE

The likelihood of ocular toxicity has been previously commented on. Thus far there are no reports citing ocular disease being due to the use of the drug. Two cases of central scotoma were reported by Kupfer *et al.*[24] but may have been incidental. No cataracts have yet been produced. Ballentine and Maren[29] reported that the lens of the rabbit treated with acetazoleamide contained too little of the drug to inhibit the enzyme. The huge amount of the latter in the lens precludes its inhibition with therapeutic doses. The possibility of visual dysfunction based on disturbance of retinal acid-base balance has been investigated by Breinin and Miller[30] using electro-retinography and dark-adaptation studies without any evidence of alteration by the drug. The fact that we have seen no derangements of ocular tissues or function does not rule out the possibility that these may result in the course of time with chronic acetazoleamide medication. The residual uncatalyzed secretion doubtless is a safety factor. Patients on prolonged therapy, however, should be carefully observed at regular intervals.

Another much cited potential disturbance is the possibility of closure of outflow channels or disuse atrophy due to inhibition of aqueous flow.

The fact that acetazoleamide is ineffective locally forces its systemic use and thereby the inevitable accompaniment of side reactions and potential toxicity. Unless its use can be confined to the eye it will always labor under a severe disadvantage. Much work must be done on this problem.

SUMMARY

1. Acetazoleamide is an important agent in the control of glaucomas of all types but is best suited to short term administration.

2. Its use in long term administration is limited by a high incidence of side reactions and difficulty in maintaining control.

3. Its virtues and failings are discussed at some length and additional applications described.

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Clinical Practice

ACCOMMODATION AND REFRACTION

METHODS OF CORRECTING LOW VISION

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The methods of correcting low vision are best classified as corrections for distance and corrections for near. Corrections for distance are much less frequently of benefit to the patient. The types of corrections for distance are: (1) regular corrections, (2) non-optical method, (3) telescopic spectacles, (4) contact lenses, (5) pinhole spectacles.

A regular correction is the result of a careful refraction. It is surprising how many patients with low vision can have their vision improved by the use of ordinary lenses. Most albinos require strong corrections. Frequently aphakic patients are found without correction.

A non-optical method of correction for low vision is frequently unwittingly utilized by the patient, as when a patient with 3/200 vision states that he enjoys television by sitting about 2 feet from the screen.

This is explained by the fact that the patient appreciates a magnification of 2× by advancing from 20 feet to 10 feet from the screen. A magnification of 10× is achieved by advancing from 20 feet to 2 feet from the screen.

Contact lenses are sometimes indicated in keratoconus, corneal scars, keratitis and choric-retinal degeneration associated with high myopia.

Telescopic spectacles are not of much value in the average patient because the magnification is about 2.2× and the field is reduced to about 12 degrees. Rarely can a patient walk with telescopic spectacles because of the rapid motion parallax and apparent closeness of objects. Pinhole spectacles are sometimes useful for corneal scars, lens opacities and dense vitreous opacities.

Low vision lenses are much more frequently useful to improve vision for near. They can be classified as: (1) non-optical method, (2) regular corrections, (3) strong plus reading additions for binocular use, (4) strong plus lenses for monocular use, (5) strong monocular bifocal for general use, (6) new magnification reading bifocal, (7) half-eye glasses for binocular or monocular use, (8) microscopic bifocal, (9) doublet magnifier, (10) telescopic spectacle with reading addition, (11) contact lenses with regular reading addition.

The non-optical method of magnification is applicable for near vision in the same relation as it is for distance. This explains the ability of young patients

with low vision to read because they are able to hold the book as close as 4 inches from their eyes. The highly myopic patient with a chorio-retinal degeneration often reads small print at a distance of 2 inches from his eyes. This produces a magnification of 10×. The use of strong plus lenses, microscopic bifocals and doublet magnifiers produces magnification by making it possible to read at distances close to the eye, e.g., a doublet lens composed of two +40.00 diopter lenses adjacent to each other in a rim produces a magnification of 20×. The patient must hold the reading material at ½ inch from the doublet lens which is the focal distance of the total of +80.00 diopters.

Regular corrections are often beneficial. Patients sometimes require a strong cylindrical combination or aphakic corrections for near which were not prescribed when the distant correction was given.

Binocular corrections for near in the form of near vision lenses, bifocals or half-eye glasses are frequently adaptable. They range in strength from +4.00 to +10.00 reading additions and are indicated for patients with binocular vision. Care must be taken to see that the lenses or bifocal segments are sufficiently decentered for the reading distance. A good general rule is to decenter the reading correction in the same amount as the reading addition, e.g., if the reading addition is +7.00, each reading lens or bifocal segment should be decentered in 7 mm.

Strong plus lenses for monocular correction are frequently applicable. A correction stronger than +8.00 or +10.00 cannot be tolerated for binocular use. Therefore stronger corrections can only be worn monocularly. If the patient has binocular vision the patient must learn to suppress the other eye, close it or wear an opaque occluder. A strong monocular bifocal for general use is often very desirable. Reading additions ranging from +10.00 to +20.00 can be worn constantly in the form of an ultex B.

The new magnification reading bifocal is intended to be used as a reading lens. This is a one piece bifocal with a 25 mm. spot ground on the outer surface of the lens. The surrounding lens is plano or contains the distant correction. These are made by the American Optical Company. At the present time the reading additions in production are +16.00, +24,00 and +32.00 diopters. The top of the reading spot or segment should come to the upper border of the patient's pupil. The convenience of being able to look up with such strong reading lenses is very advantageous. The +32.00 diopter reading addition has been found to be preferred to the 8× doublet (+32.00) in 2 cases. Magnification is expressed by dividing the dioptic power by 4.

Half-eye glasses can be supplied for binocular use or monocular use. Half eye glasses offer the advantage of distant vision without taking the glasses off.

Microscopic bifocals are indicated for patients requiring +40.00 additions or stronger. The 10× magnification (+40.00 diopters) and 14× magnification (+56.00 diopter) are indicated for patients with very poor vision, e.g. 3/200. The top of the magnification element should come to the upper border of the patient's pupil.

Doublet magnifiers consist of 2 plus lenses adjacent to each other. The most

useful is the 12× magnification. This unit consists of two +24.00 diopter lenses adjacent to each other in a plastic rim. They are also made in 16× magnification and 20× magnification. This type of lens rehabilitated, to some degree, a number of patients who had little vision remaining.

Telescopic spectacles with a reading addition are sometimes useful. These are indicated in those situations where the reading or working distance must be the greatest possible, e.g., a shoemaker. The reading additions found to have the greatest application are +4.00, +6.00, +8.00 and +12.00 diopters. In most instances a strong plus lens supplies the same magnification and a larger field. They are much lighter as well as being less expensive and less noticeable. The only disadvantage is that the patient must hold the reading material closer to his eyes.

Presbyopic patients wearing contact lenses for distance require a reading addition which must be worn in the form of a spectacle.

Comment: During the past several years, ophthalmologists everywhere have evinced a renewed interest in the relief of individuals with severe visual disabilities. Of course, surgical procedures and medical treatment have always been employed in these cases where possible and these methods are practiced by every ophthalmologist. Supplementing these procedures is the relief of the residual visual deficiencies by means of special appliances, a field in which many ophthalmologists have been doing excellent work for many years, but with little general recognition. The tremendous increase of interest in the problems of low vision is best shown by the number of instruction courses offered during the last several years at the American Academy of Ophthalmology and Otolaryngology meetings, courses which are always crowded.

Every ophthalmologist is interested in helping those of his patients who, for one reason or another, have marked visual disability, and such cases form an appreciable percentage of the practice of the average ophthalmologist. Reduction of vision below normal, when proper correcting lenses are worn, is always the result either of primary ocular disease or of the ocular manifestations of general disease, and, as such, this field is certainly one of the major ones in ophthalmology.

It should go without saying that no effort should be made to prescribe low vision aids until an adequate ophthalmologic examination has established the absence of an active disease process, or, if the latter is present, until it is controlled sufficiently to permit the supplying of aids.

The author of this paper has presented in a concise way the indications for low vision aids and the type suitable for each condition. His experience has been wide and this has been reflected in his lack of enthusiasm for telescopic appliances in most cases. It is now becoming evident that telescopes are useful only in a very few cases of severe visual disability, and then usually only where the patient must, for occupational or other good reasons, have improved vision for distance. Occasionally, in suitable cases, the telescopic appliances may help to secure an adequate magnification at the near point without holding the reading or other material quite as close as would be necessary in obtaining the same magnification with simple magnifiers.

Many of those who need low vision aids are the wards of one of the organizations devoted to assisting the visually handicapped. In such cases, the cost of suitable appliances may not be a problem to the patient, but where the patient has no such assistance, cost may be a major consideration if commercial appliances are used. Practically, many high-

powered doublets, and even telescopes, may be made by a dispensing optician or an optical prescription house at a much lower cost than by the usual manufacturers. These, however, must usually be designed by the ophthalmologist and the specifications for them given to the laboratory. In the recent ophthalmologic literature may be found the details of the process of designing such lenses.

If cost considerations are not too important, telescopes, such as those produced by the Kollmorgen and Univis Companies, may be obtained complete with attachable caps containing the patient's refractive correction and with his addition for near. The new magnification reading bifocals may be supplied by the dispensing optician on prescription, or obtained through a prescription laboratory.

Projected magnification is a non-optical method which may occasionally be combined with optical appliances. This method is effective if vision is not too low. In the latter case, the poorer contrast resulting from the reflected projection of the printed page often interferes with vision in spite of magnification.

In all cases of severe visual disability, improved by any method, it must be kept in mind that the patient is going through an entirely new experience and should be told that he "must learn to see all over again". Usually, as a result of his efforts to adapt himself to the new situation, his actual visual ability will increase as he learns to interpret better the imperfect visual impressions which he receives. Thus the ophthalmologist must encourage the patient during this learning period, explaining to him the reason for the difficulties which he is having with the initial use of the visual aid.

EDWIN FORBES TAIT

FREQUENCY AND ETIOLOGICAL SIGNIFICANCE OF CORNEAL ASTIGMATISM IN DETACHMENT OF RETINA, PARTICULARLY WITH A TEAR AT THE ORA

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Arch. f. Ophth. 1956, *157:* 592–597

Measurements of refraction were performed on 1065 eyes with detachment of the retina, 248 of which had a tear at the ora. It was found that corneal astigmatism in general, unilateral astigmatism, and oblique direction of the principal meridians of the cornea occurred twice as frequently in these eyes than in normal eyes. Unilateral corneal astigmatism in the eye with detachment of the retina occurred more frequently in the presence of a tear at the ora, than in the presence of other types of tears. These findings were statistically significant. Dysontogenetic development of the primitive epithelial papilla and of the retina are to be considered as the common partial cause of the simultaneous occurrence of detachment of the retina and corneal astigmatism. These defective embryonal developments may explain the preponderance of the lower temporal location of

the tear in the ora and the preponderance of the involvement of the right eye. In a large number of cases of simultaneous occurrence of detachment of retina and corneal astigmatism there is a similar causative relationship as in the genesis of myopia.

Comment: This paper is a small but interesting link in a chain of thoughts expressed by various investigators during the past decade bearing upon the genesis of a variety of not obviously related clinical conditions, such as myopia (BADKE, G., Arch. f. Ophth. 1952, *153:* 231), hereditary segmental cystic degeneration of the retina with predisposition to hole and tear formation (YAEGER, W., Klin. Monatsbl. f. Augenh. 1955, *127:* 423), and possibly also keratoconus and keratoglobus.

The concept of maldevelopment and a genetically determined inferiority of tissues has been introduced to explain some of clinical behavior of ocular structures. Some findings, for example, suggest a genetically determined myopic retina with an inherent tendency for overgrowth of the neural ectoderm and an increased number of percipient retinal elements in the embryonic "Anlage," and later a correlated anomalous growth of the sclera. The well-known inferiority and reduced vitality of malformed tissues would make possible further limited damage by mechanical forces.

BERTHA A. KLIEN

THE LENS

EPITHELIAL INVASION OF THE ANTERIOR CHAMBER

A. Edward Maumenee and C. Richard Shannon

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Trans. Pacific Coast Oto-Ophthl. Soc., 1955, *36:* 107–135

The presence of ectodermal epithelium in the anterior chamber causes troublesome ocular complications. The present report is based on 11 cases of this type treated or observed by various staff members of Stanford University Hospital.

EPITHELIAL PEARL TUMORS OF THE IRIS

This type of tumor is rarely encountered. The lesion usually results from the implantation of a hair follicle or a piece of skin in the anterior chamber at the time of a perforating injury. Clinically, it appears as a solid pearly tumor or opaque white cyst on the surface of the iris, not connected with the wound of entry into the anterior chamber. The mass grows slowly and may not attain a size of more than 2 to 3 mm. in diameter in some cases. In others it may fill most of the anterior chamber or extend into the posterior chamber. Frequently it causes a mild iridocyclitis.

If the tumor increases in size or causes iridocyclitis it should be removed by performing a complete iridectomy in the area of the mass. When the entire tumor is removed the prognosis is good, but if only a part of the lesion is excised it may recur, secondary glaucoma may develop and the eye may be eventually lost from intractable pain.

EPITHELIALIZATION OF THE ANTERIOR CHAMBER OR EPITHELIAL DOWNGROWTH

The incidence of epithelial downgrowth into the anterior chamber following perforating injuries or surgical procedures is difficult to determine from the literature for many authors have not clearly stated whether the lesions they have described were true epithelial downgrowths or merely epithelial cysts. A clear example of the incidence is obtained from the study of 75 eyes enucleated following cataract extraction at the Illinois Eye and Ear Infirmary, of which 14 (18 per cent) demonstrated epithelial invasion of the anterior chamber.

The lesion occurs most frequently following poorly performed cataract extractions where the anterior chamber has not been properly closed and either the anterior chamber has remained flat or the eye soft for several days or weeks after extraction. In cases where epithelium invades the anterior chamber a thin translucent membrane can be detected on the posterior surface of the cornea. A most important finding is a fine gray line just at the lower border of this mem-

brane. Surface epithelium also covers the iris underlying the area of corneal involvement. In such regions there is a slight loss of normal iris markings and with careful examination with high magnification a thin film may be seen on the anterior surface.

A number of lesions may be mis-diagnosed clinically as epithelial downgrowth. Some of these are (1) a markedly shelving corneal section; (2) vitreous in contact with the posterior surface of cornea; (3) invasion of the anterior chamber by sub-epithelial connective tissue and blood vessels; (4) a peeling off of Descemet's membrane from the cornea above; (5) a glassy membrane, or re-duplication of Descemet's membrane.

POST-TRAUMATIC OR EPITHELIAL CYSTS OF THE ANTERIOR CHAMBER

Epithelial cysts characteristically appear as translucent or grayish cysts which are connected, at least at one point, with an area of penetration into the anterior chamber. The cyst may lie dormant for years or it may grow to considerable size and then remain stationary without causing further damage.

In surgical treatment the cyst whould be aspirated and collapsed with a 24- to 27-gauge needle. When this is done it is possible to determine where epithelium is firmly adherent to the posterior surface of the cornea and where it is merely in apposition. The cyst should then be approached through an *ab externo* incision. The unattached cyst wall is removed with intracapsular cataract forceps and the epithelium removed from the back of the cornea by gentle curettement or swabbing with an applicator moistened with 70 per cent alcohol. A large iridectomy should be done over the area where epithelial tissue is adherent to the surface of the iris.

Comment: This is the most comprehensive article that has appeared on this subject within the past few years. As the authors state, the clinical diagnosis of epithelial downgrowth is extremely difficult to make. The true diagnosis is usually made in histologic section. There is no question that it usually follows some failure in technique at the time of cataract surgery. Faulty closure of the wound, too deep sutures, or the introduction of tissue into the eye while repositing the iris may cause epithelial downgrowth or may lead to epithelial cysts of the anterior chamber.

One wonders why in some cases epithelial cysts develop and in other cases epithelial downgrowth occurs. The reviewer has seen several cysts following penetrating wounds but has never seen epithelial downgrowths other than after cataract surgery.

The treatment recommended by the authors would appear to be the treatment of choice. The use of electrodiathermy and electrolysis has its advocates and undoubtedly is successful in certain cases—especially in small cysts. The reviewer has on two occasions attempted surgical removal after repeated attempts of cyclodiathermy have failed. The operation has been complicated by adherence of the cyst to the areas of penetrating diathermy as well as adhesions of the cyst to the hyaloid. One eye was finally enucleated and in the other, though the cyst did not recur, useful vision was not obtained. In four cases of primary surgical removal, two of which occupied ⅓ to ½ of the anterior chamber, the final result was excellent. The operation is simpler and less likely to cause complications in the phakic as compared with the aphakic eye. Needless to say the earlier the operation is done, the easier it will be to perform.

P. Robb McDonald

LATE SURGICAL RESULTS OF USE OF THE INTRAOCULAR ACRYLIC LENS

HAROLD RIDLEY

London, England

J. Internat. Coll. Surg., 1956, *26:* 335–341

All the patients who underwent the intraocular acrylic lens operation in the general wards of St. Thomas's Hospital in 1951, 1952, and 1953 were sent for in 1956 and most of them appeared and were examined and refracted. It was found that after a long postoperative period rather more than one-half of the eyes retain corrected acuity of 6/12 (20/40) or better, one-third 6/9 (20/30) or better, and one-quarter 6/6 (20/20) or better. These proportions show some deterioration when compared with those published in 1954, after a shorter postoperative interval, when two-thirds had 6/9 and one-third 6/6 vision, and with those of the 1955 series in which two-thirds had 6/12 and one-half 6/9 or more.

Judged on visual acuity alone, these results are inferior to those of plain extraction, but it must be emphasized that postoperative central acuity is not the only criterion by which the operative results should be compared. The acrylic lens does not magnify the image by one-third, so that, in a patient with an acrylic lens 6/9 acuity is really equivalent to 6/6 through an aphakic correction. Moreover, a lens in the natural position provides natural sight with a full undistorted visual field. The eye can be used together with the other eye, which may be slowly deteriorating, and heavy and unsightly cataract glasses are not necessary to provide even moderate sight. In some patients, especially those with monocular cataract, natural vision even with as little as 6/18 acuity may be adequate and indeed preferable to a better central acuity obtained with the aid of strong lenses. Reading sight with an intraocular acrylic lens is often surprisingly good, and there are few eyes which cannot read small print even if the vision for distance is only moderate.

In cases of monocular cataract, the incidence of preoperative complications, such as traumatic subluxation or uveitis, which may adversely affect the result, is likely to be greater than average. In general, the cause of failure, when it occurs, is usually evident, late dislocation in which the lens slides behind the iris into the base of the vitreous chamber being the complication most to be feared. Fortunately, the acrylic lens, when dislocated into the vitreous, is better tolerated than is the human lens, and good acuity with a cataract glass may result. If the other eye is normal, however, this is not of much practical value.

Late dislocations occurred in four patients. The first, a boy aged 12, had an anterior dislocation resulting from a blow on the eye from a fist, after six months with an acuity of 6/9. The others were spontaneous posterior dislocations; in one at least the posterior lens capsule was inadvertently removed, and in the other two it may have been. Posterior dislocation of the lens cannot occur unless the posterior capsule or zonule has been torn, and it seems probable that, in the

absence of a blow on the eye, most if not all such rents are caused at the time of the operation or, in cases of traumatic cataract, before it. It is not certain that spontaneous posterior dislocation of an acrylic lens has ever occurred with the zonule and posterior capsule intact when the lens was inserted.

Incomplete removal of all lens matter at operation seems to be the most common and important surgical fault, and failure should be expected unless a perfect extracapsular extraction is performed before an acrylic lens is inserted.

A dense posterior lens capsule, inflammatory deposits on the front of the lens, subluxation, and corneal trauma were apparently the reasons for the merely moderate visual results in one-fourth of the patients; in two others, the cause was obscure.

The method of cleaning and sterilizing the lens by immersion in 1 per cent cetrimide has been criticized. In actual practice, however, it seems that little trouble has been attributable to it. Postoperative iritis appears to be associated with the extracapsular technique and the retention of cortical and capsular lens remnants within the eye rather than with the acrylic material or the cetrimide.

A dense inflammatory membrane can be divided, as in capsulotomy, and this has been done in seven of the cases in this series, often with most gratifying results, for the lens is generally quite clean beneath the pupillary membrane. An operation originally successful seldom gives serious trouble unless dislocation occurs, and the patient can retain good sight without evidence of foreign body reaction or degeneration of intraocular structures for at least five years and probably indefinitely. No more effective treatment for monocular cataract has yet been devised, and if a safe method could be invented for fixing the lens securely in the patellar fossa to prevent posterior dislocation, the risk of late complications would probably be comparable to that associated with plain extraction.

Comment: This report is of interest since it concerns patients with a follow-up period of 3 to 5 years. The statistics are based on 41 patients. When one considers that there were four posterior dislocations (approximately 10 per cent), and that four other patients had less than 6/60 vision (10 per cent), (one eye being enucleated and one having no light perception), the attrition rate would appear to be rather high. (Thirteen patients had more than one surgical procedure; i.e., corepraxia, capsulotomy, division of posterior synechiae, etc.). Undoubtedly, as in any new procedure, the selection of cases and the operative technique was not as well established in 1951 as it was several years later. One is inclined to ask, What price for undistorted vision and the avoidance of cataract lenses?

Reese and Hamde (personal communication) have performed over 100 acrylic implants with much better results than those reported in this paper. This reviewer has had occasion to see several of their patients and has been impressed with their results and the apparent lack of postoperative reaction. There is no question, however, that full pupillary dilatation is difficult and should these patients develop retinal detachments, the prognosis for a successful result would be markedly reduced because of the inability to examine the peripheral fundus.

This is obviously not an operation for the occasional operator and it would probably be better for most of us to allow a few to learn and report on the pitfalls of this bold but intriguing surgical procedure. It may well be that the answer will be a plastic lens

inserted in the anterior chamber in such a manner that it could be removed if necessary and posterior dislocation would be impossible.

P. Robb McDonald

HISTOPATHOLOGIC STUDIES OF EYES ENUCLEATED AFTER FAILURE OF INTRAOCULAR ACRYLIC LENS OPERATIONS

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Brit. J. Ophth., 1956, *40:* 473–479

The most prominent feature revealed by histopathologic examination of nine eyes enucleated after Ridley's acrylic lens operation is the invariable presence of a large amount of fibrous tissue in the anterior segment of the eye which is usually visible macroscopically as a pseudocapsule for the lenticulus. Microscopically, its anterior layer is adherent to the disorganized posterior aspect of the iris, in which pigment disturbance is a marked feature, and its posterior layer is usually but not always adherent to the remannts of the cataract. Giant cells were seen in three specimens only, but eosinophils were found in all but one case, sometimes in enormous numbers.

The picture is frequently complicated by mechanical factors such as incarceration of iris remnants in the operation wound, or, as in one case, by frank infection, or, as in four other cases, by the prior removal of the lenticulus, so that it is difficult to establish the precise role played by the implant in the pathologic picture. On the basis of these studies, however, it seems that proof of the irritating nature of the material of which the lens is made (fully polymerized polymethyl methacrylate; Transpex I) is not yet available, since the factors of mechanical or antiseptic irritation have not been excluded. It is notable, however, that one pathologic change which is present in all the specimens, namely, the deposition of fibrous tissue in the immediate vicinity of the acrylic lens, does not seem to be influenced by the time during which the lens remains in the eye. In the three last cases, in which the implant had been retained for longer than six months, there was no increase in fibrous tissue as compared with the previous six cases in which the lens had been retained for shorter periods. It is tempting, therefore, to speculate that the noxious stimulus causing the fibrotic reaction may not be the lens itself, for, if it were, an increase of fibrous tissue formation would be expected in the longer-term cases. The findings suggest, rather, that the stimulus is possibly some substance adherent to or part of the acrylic lens, which, having been liberated and having caused an inflammatory

response, becomes expended. In this connection it is of particular interest to know to what degree the acrylic material absorbs cetrimide 1 per cent, the antiseptic recommended by Ridley for sterilizing the acrylic. There is no doubt that the fibrosis of the anterior segment of the globe is the specific pathologic change in these cases, and if it could be avoided by the use of alternative methods of sterilizing the lenticulus, a considerable advance would have been achieved.

One important question is whether the appearances would be similar in a successful case, since it must be remembered that the present series consists of unsuccessful cases only and therefore tends to give an unduly gloomy picture. Information about one successful case, in which the eye became available for examination through the death of the patient, has been provided by Rintelen and Saubermann (see the following condensation, Ed.). In this successful case, as in the present series, there was a fibrous membrane, containing pigment particles, adherent to the posterior surface of the iris and to the anterior aspect of the lens remnants.

Comment: After reading this review there are probably many ophthalmologists saying to themselves or others, "I told you so!" Before being too critical one should know what percentage this is to total number of acrylic implants performed in England. One should also know something about the selection of cases and if the surgeons had previous experience in the operative procedure. It is only human nature to want to try something new and likewise in a bold procedure such as this, one may at first attempt it in a less than ideal case where the patient has something to gain but not everything to lose.

There seems to be little question that the acrylic lens is responsible for a rather marked inflammatory response. This undoubtedly varies from patient to patient and may depend on several factors: sensitivity to retained lens material, sensitivity to the plastic or the sterilizing solution, etc. The use of corticosteroids locally inhibits the reaction to a considerable degree and it is doubtful if the operation could be performed without the help of these anti-inflammatory drugs.

P. Robb McDonald

PATHOHISTOLOGIC STUDIES AFTER IMPLANTATION OF PLASTIC LENSES IN MAN

F. Rintelen and G. Saubermann

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Ophthalmologica. 1956, *131:* 369–373

Implantation of a plastic lens was carried out in the eye of a 70-year-old woman with a mature cataract. One and a half years later the patient died of carcinoma of the breast, autopsy was performed and the patient's eye was studied microscopically within five hours after her death.

The choroid showed carcinomatous metastasis; there was cystoid degenera-

tion of the periphery of the retina, senile atrophy of the ciliary body and considerable cadaverous changes. But these were secondary findings in so far as the implantation of the plastic lens was concerned. With regard to the consequences of the implantation of this lens in the eye, the following observations were made:

(1) At the time of the patient's death the plastic lens did not cause even the slightest inflammatory reaction of the tissues in the adjacent and in the more distant areas.

(2) After the implantation an inflammatory reaction with connective tissue-like organization of the exudate had occurred. This reaction apparently was limited to the posterior surface of the iris and its pupillary portion.

(3) The posterior surface of the iris, apparently, had been injured at several sites in the course of the operation. The extensive membrane-like scar formation which was observed on the anterior surface of the plastic lens was explained by the operative lesions of the iris and by the fact that considerable portions of the anterior capsule of the lens, and of the capsular epithelium underlying it, had remained. Inflammatory reactions occurred only in areas in which the plastic lens had come in contact with the injured posterior surface of the iris.

(4) The postoperative hyperemia of the iris, together with flattening of the anterior chamber after the implantation, resulted in a circular synechia of the root of the iris with the corneoscleral trabeculum. This change might have caused a secondary glaucoma later.

(5) The cortex of the lens had been completely removed at the operation.

(6) The limiting membrane of the vitreous was not injured in the course of the operation and such a lesion did not occur as a sequela of the operation.

(7) An occasional discission of an aftercataract or removal of the newly formed pupillary membrane must be performed before the organization of a solid scar and adhesions occur.

(8) The observed synechia of the root of the iris showed that a certain reserve is advisable in evaluating long term results after implantation of a plastic lens.

The authors, however, consider it most important that the plastic lens was well tolerated by the eye. They emphasize the importance of the extensive removal of the anterior capsule of the lens and of its epithelium, and the prophylactic prevention of injuries of the iris in order to prevent the undesirable occurrence of aftercataract. The microscopic findings in the case reported on, are altogether encouraging the authors to continue with the implantation of plastic lenses according to Ridley's technique.

Comment: Within the knowledge of the reviewer, this is the first published histologic report of a successful Ridley implant. The author employed a complete iridectomy, which is not generally used. The inflammatory exudate on the posterior surface of the iris apparently helps in maintaining the lens in its proper position. The inflammatory reaction varies as to the amount of capsular epithelium remaining, and, to the trauma to the iris at the time of operation. This, associated with hyperemia of the iris and flattening of the anterior chamber, caused some peripheral anterior synechiae.

The authors' conclusions are well taken and they would appear to be well aware of the potential complications that may occur.

P. Robb McDonald

LUXATION OF THE LENS INTO THE VITREOUS BODY

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Klin. Monatsbl. f. Augenh. 1956, *128:* 573–580

Dislocation (luxation) of the lens into the vitreous body is a serious complication of a congenital condition (Marfan's syndrome) or of trauma, and it presents a great danger to vision. Many surgeons caution against the extraction of the lens which, they believe, offers little prospect of visual improvement. They limit surgical intervention to the control of secondary glaucoma which is frequently associated with the luxation of the lens.

Contrary to these views, Kreibig states that antiglaucomatous measures are of doubtful efficiency in cases of this type, and he recommends a more active procedure which he employed successfully in eight patients with traumatic dislocation of the lens in the vitreous. The extraction of such a dislocated lens is difficult only because one may not make the lens visible as it floats about freely in the vitreous.

The author's method consists of the usual cataract incision followed by total iridectomy. Then the edge of the lens is sharply focused with the aid of the electric ophthalmoscope. A wire loop is carefully inserted under the flap of the conjunctiva and is introduced through the incision into the interior of the eye; the wire loop is brought close to the edge and slipped slightly under the edge of the lens. By lowering the handle of the loop, the lens can be lifted and removed. The extraction of the lens thus was successfully performed in all the patients and the unavoidable loss of the vitreous remained within moderate limits. Slight postoperative gaping and elevation of the conjunctival flap by a fragment of the vitreous occurred and continued for several days in one patient only. In all the others, agglutination of the wound was satisfactory and exact immediately after the intervention. This was due to the fact that the entire surgical intervention was terminated within a few minutes. In cases of luxation of the lens after trauma, surgical intervention should be performed immediately when liquefaction of the vitreous has not occurred.

Comment: "To be or not to be, that is the question." It is true that many ophthalmologists will leave a dislocated lens in the vitreous providing the eye is quiet; surgical intervention being reserved for those eyes with evidence of a cyclitis or secondary glaucoma. The rationale for an attitude of watchful waiting, is that some eyes will tolerate a luxated lens for years; that the surgical removal, though successful in its objective, is frequently followed by severe complications as secondary glaucoma and retinal detachment. The basis for removing the lens is that if one waits for complications to occur, they are not always relieved by the surgery and one may encounter the same complications as if it were removed when the diagnosis was first made.

The use of an ophthalmoscope to locate the lens would appear to be as valuable an aid as the ultraviolet lamp. One should certainly never go searching blindly with a loop. The

reviewer cannot agree with the author that it is important to remove the lens before liquefication of the vitreous has occurred. One can usually remove a lens from a fluid vitreous with greater facility and less trauma than in an eye with formed vitreous.

Cases of this type require surgical acumen as well as dexterity. Each patient must be carefully evaluated keeping in mind he may eventually lose the eye, but it may be better to gamble on several months of seeing rather than a few short days following his operation. Should operation be decided on, one should be prepared for loss of vitreous, precautions should be made to keep it at a minimum and after firm closure of the wound with several sutures, vitreous should be cleared from the wound with air in the chamber and with a spatula, if necessary.

P. Robb McDonald

THE CONJUNCTIVA AND CORNEA

PIGMENTED TUMOURS OF THE CONJUNCTIVA

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Tr. Ophth. Soc. Australia, 1955, *15:* 128–143

Pigmented tumors of the conjunctiva and intraocular melanomas, with which they have little in common, should be considered separately in the interests of clear thinking. In general, the pigmented tumors may be classified as follows:

A. Benign:
   - Deep (or intradermal) nevus.
   - Junctional nevus and compound nevus.
   - Juvenile melanoma.
   - Blue nevus.

B. Precancerous:
   - *Lentigo malignum* (Becker).
   - Activated junctional nevus (Allen and Spitz).
   - Precancerous melanosis (Reese).

C. Malignant:
   - Malignant melanoma or melanocarcinoma, (*a*) superficial (including cancerous melanosis of Reese), (*b*) deep.
   - Malignant blue nevus.

The term intradermal nevus, used for tumors of this type when they occur in the skin, obviously cannot be applied to lesions occurring in the conjunctiva and the term deep nevus is therefore to be preferred. It indicates that the nevus cells are present only in the submucosa. Clinically, these nevi are usually elevated, reasonably circumscribed, and deeply pigmented. The histologic picture

is characterized by the fact that the overlying epithelium is intact and without evidence of junctional proliferation, and that a zone of collagen intervenes between the epithelium and the deep neval tissue, the cells of which are arranged in nests and cords. This picture is modified when the lesion appears at the limbus, so that the nevus tends to be flatter and more superficial in location. It is important to distinguish the deep nevus from other types because there is good reason to believe that it rarely if ever becomes malignant. When deep nevi occur in the conjunctiva, they lack clinically distinguishing features and they can be identified with certainty only by biopsy and section.

The junctional nevus is formed at the junction of the epithelium with the submucosa by proliferation of melanoblasts in the basal layers of the epithelium. Conjunctival nevi are usually sharply demarcated, almost always elevated to some extent, and exhibit an undulating, irregular surface. At times, slit-lamp examination may be needed to detect the elevation. Occasionally, these nevi may be quite flat and diffuse, presenting clinically as a flat area of brown staining closely simulating precancerous melanosis. Histologically, junctional nevi are recognized by the clusters of proliferating melanoblasts in the basal layers of the epithelium. These are the nevus cells and though they have a tendency to drop down into the superficial submucosa, this movement is a normal process in the natural evolution of the growth and the migrating cells are benign in character and morphology. Nevertheless in both junctional and compound nevi, in which deep nevus tissue is associated with junctional proliferation in the overlying epithelium, the epithelium is in a state of unrest that may be the starting point for malignant change.

Nevi have been classified according to their degree of activity. Unfortunately, different authors have used different criteria and different terms, so that the nomenclature has become confused. Certain conclusions can be drawn, however, from a study of junctional nevi and their allied lesions. (1) In quiescent nevi the movement of the nevus cells is predominantly downward into the superficial submucosa. (2) The most constant histologic sign of activity in a nevus is the migration of proliferating cells, both singly and in groups, upward towards the surface. (3) Malignant conversion originates in the junctional zone and proceeds by perverted junctional proliferation, which produces not benign nevus cells, but anaplastic cancerous cells. These express their malignant character by actively invading the submucosa, where they excite an inflammatory response. Since it seems unlikely that benign nevus cells themselves undergo malignant change, it would probably be truer to say that malignant conversion begins in an area of junctional unrest rather than that a nevus becomes malignant. (4) In interpreting lesions or tumors that are on the borderline, the histologist must answer two questions: (1) Are the proliferating cells anaplastic? and (2) Have they penetrated the submucosa? If the answer to both is yes, the tumor is a melanocarcinoma and requires radical treatment. If the proliferating cells are anaplastic but wholly intraepithelial in location, the lesion is in its precancerous phase and probably therefore more amenable to treatment.

Precancerous melanosis may be defined as a pigmented intraepithelial car-

cinoma analogous to the intraepithelial carcinoma of bowen. If left untreated, it will probably in most cases develop into a metastasizing malignant melanoma or melanocarcinoma. It is not preceded by a nevus but is acquired as a newly appearing lesion in adult life. The precancerous phase commonly lasts from five to ten years, after which one or more malignant foci develop either simultaneously or successively. Precancerous melanosis may require differentiation from pigmented junctional nevus, congenital melanosis, and the rare condition known as ochronosis.

Juvenile melanomas, which present a very difficult diagnostic and therapeutic problem, are fortunately rare in the conjunctiva. Though histologically malignant, they are clinically benign in most cases. Blue nevi, too, rarely occur in the conjunctiva. Malignant transformation of these lesions with metastases has been reported but is exceptional. Melanocarcinomas are derived in most cases from a preexisting lesion, though a few may arise *de novo*. Analysis of the author's series of 153 pigmented conjunctival lesions suggests that melanocarcinomas of the conjunctiva not infrequently originate in preexisting nevi. This is at variance with the views of Reese, who believes that malignant conversion in a pigmented nevus is rare and that the great majority of malignant melanocarcinomas are derived from precancerous melanosis. The importance of precise histologic diagnosis as a guide to the rational treatment of conjunctival pigmented tumors and melanoses cannot be too strongly emphasized.

Comment: Greer's classification of the pigmented tumors of the conjunctiva into three groups, benign, precancerous and malignant, is along classical lines and simplifies one's thinking in this complex group of lesions. His experience with melanocarcinomas arising from pre-existing nevi will arouse interest on the North American continent where the teachings of Reese have been followed. Malignant change occurs mostly in the junctional type of nevus, and the author points out that the change probably occurs in an area of junctional unrest rather than in the nevus itself. His series contained 13 malignant tumors of nevus origin out of a series of 153 pigmented conjunctival lesions.

This paper is worthy of study by the student of pathology who finds himself lost in a confusion of descriptive terms. It is equally of value to the clinician who is constantly perplexed by the inadequacy of our present knowledge of these lesions, and for whom the descriptive literature may not be helpful in individual cases.

HUGH L. ORMSBY

THE OCULAR MUSCLES

TREATMENT OF AMBLYOPIA EX ANOPSIA WITH ECCENTRIC FIXATION

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J. Iowa M. Soc., 1956, *46:* 449–455

In some patients with uniocular strabismus, the deviated eye makes no movement of redress, but remains in its deviated position when the fixating eye is occluded. Such eyes usually have an absolute central scotoma and very low visual acuity, and are generally said to have eccentric fixation. This condition, which represents a form of amblyopia ex anopsia, poses special problems with regard to both its nature and its treatment. The view that there is a close connection between anomalous (secondary) retinal correspondence and eccentric fixation has been adopted by various authors, including Duke-Elder, although he warns that anomalous correspondence is by no means confined to and does not essentially depend upon the perversion of fixation.

These concepts of eccentrix fixation, however, have never greatly appealed to the author. He believes that emphasis should be put on the poor central vision and thinks that true eccentric fixation does not occur in these patients. The true situation can perhaps best be described as follows: In the alternate cover test, which makes use of the re-fixation reflex, the patient assumes central fixation with either eye, provided that by so doing he obtains a clearer view of the fixation point than he would if the eye remained deviated. If the vision of the macular area is so far depressed that its acuity is below that of the peripheral retinal area on which the fixation point is imaged when the eye is deviated, there will be no movement of redress, since it would entail no reward. The terms false macula and pseudomacula cannot be considered appropriate, because the peripheral retinal region in question neither has nor acquires macular characteristics. Moreover, it is misleading and confusing to attempt to establish a close relationship between eccentric fixation and anomalous correspondence. Although many patients with eccentric fixation undoubtedly have anomalous correspondence, the two phenomena are quite distinct in nature and origin.

Regardless of the nature of eccentric fixation, the question whether complete and constant occlusion is a proper form of treatment in these patients remains open. In this country, ophthalmologists interested in the treatment of amblyopia have repeatedly insisted that occlusion as such is a passive procedure which is of no avail unless the amblyopic eye is actively used. Attempts have therefore been made to supplement occlusion with simple, planned exercises that can be done at home. Whether the very elaborate methods of exercise advocated by Bangerter are really more effective remains to be seen.

Because of the practical importance of the problem, the dearth of clinical material available in the literature and the existing differences of opinion, a survey of patients with eccentric fixation returning to the strabismus service and the orthoptic department of the Department of Ophthalmology of SUI has been started. So far, the records of 35 patients with eccentric fixation to whom occlusion treatment in one form or another was given have been collected. For purposes of comparison, the records of seven patients who had very low visual acuity in their amblyopic eyes but who fixated centrally have also been included. The number is still too small for statistical evaluation but certain conclusions may be drawn from the study as a whole. In no case did it appear that occlusion of the better eye reduced the chances of improving the vision of the amblyopic eye. The acuity of the amblyopic eye was in fact more or less significantly improved in most cases. Important factors influencing the result of the treatment were the age of the patient and the degree of his cooperation. The younger the child at the start of the treatment, the better the result. When cooperation was poor, there was no gain in visual acuity, but when cooperation improved the gain was often remarkable. Nothing less than total occlusion was of any avail, although temporal occlusion of the amblyopic eye was of some use as a preliminary measure in a number of cases. The visual acuity of patients with eccentric fixation, even when improved to as much as 6/6, tends to slip back more readily than does that of patients who start out with central fixation and this makes it necessary to follow them closely for longer periods. In a few patients, a boost in visual acuity followed surgical straightening of the amblyopic eye after central fixation had been attained.

From this material it seems that the diffence between amblyopia ex anopsia with eccentric fixation and amblyopia with central fixation is one of degree only.

Comment: The crux of the dispute about the value of occlusion in cases with eccentric fixation depends upon the criterion for deciding if a patient does or does not have eccentric fixation. I do not believe that the fact that a patient with uniocular strabismus makes no movement to take up fixation with the deviated eye when the fixating eye is occluded is proof of eccentric fixation. As Dr. Burian states, this merely indicates that the central acuity is so low that there is no reward for shifting fixation to the central area. In these cases, if (while the fixating eye is occluded) one moves a small object of interest in front of the child and the child is instructed to touch this with one finger, the child will then shift fixation. Depending upon whether the eye takes up central or slightly eccentric fixation at the edge of the dense central scotoma, one decides about the type of fixation. If the child selects the same eccentric area on repeated trials, one makes the diagnosis of fixed or obligatory fixation. In these cases, constant and complete occlusion is of no benefit as the child will continue to fixate with this same eccentric area. If the child does not fixate centrally but chooses various eccentric areas to fixate (wandering eccentric fixation), the prognosis for success with occlusion is much better.

PHILIP KNAPP

CÜPPERS AFTER-IMAGE METHOD IN THE TREATMENT OF ECCENTRIC FIXATION

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Ophthalmologica, 1956, *131:* 261–262

Occlusion of the healthy eye is indicated in patients with amblyopia and central fixation. This occlusion is contraindicated in patients with amblyopia and eccentric fixation, because it would accenuate the eccentric fixation.

The euthyscope is an ophthalmoscope with a broad bright cone of light with the central area covered. The fundus is illuminated with the euthyscope for several seconds while the macula is covered. A positive after-image appears and this is followed closely by a negative after-image. With the latter, the area spared by the cover mark appears as a bright spot in the midst of a dark field. Herewith the direction of vision of the macula becomes subjectively recognizable in space and can be trained.

The following considerations should be applied concerning the development of eccentric fixation: The occurrence of double images must be expected with strabismus. To prevent this occurrence, the visual impressions of the squinting eye are inhibited, and particularly those of the area of the macula. A relative central scotoma results, and herewith amblyopia. Macular fixation may be lost with a strongly developed central scotoma. Then two types of fixation develop: (1) the completely missing or changing fixation; (2) the localized eccentric fixation.

The prognosis is favorable for the first type, but unfavorable for the second type as this false fixation becomes a habit and the closer it is to the proper macula. This prognosis also depends on the quality of the after-image: This should last as long as possible. By flicker-illumination of the exercise-room, a prolongation of the after-image can be achieved.

The control of fixation is carried out with the star test of the visuscope. At this time, direct perimetry of the relative central scotoma at the fundus can also be performed.

The prerequisite for the success of this method is the occlusion of the amblyopic eye. When the amblyopic eye no longer receives visual impressions, the inhibition impulse becomes purposeless; the inhibition itself recedes. Simultaneously the eccentric fixation is destroyed. As a rule, therefore, the amblyopic eye is to be occluded for at least three weeks before treatment is started and for the entire treatment period, until central fixation is obtained. From this time on, the healthy eye must be occluded. The squinting position must be either removed surgically, or the monocular strabismus should be converted in an alternating type, because vision may otherwise be diminished again.

Treatment itself requires daily sessions for three to six weeks; treatment cannot be practiced in children before the ages of 8 to 10 years. The method can be

successful in adults likewise, but one should be aware that beyond the age limit of about 15 years, binocular vision can no longer be obtained.

USE OF BIFOCAL SPECTACLES IN THE TREATMENT OF ACCOMODATIVE ESOTROPIA

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Brit. Orthoptic J., 1956, *13:* 3–6

Bifocal spectacles are a valuable adjunct in the treatment of accommodative esotropia. They assist in keeping the children's eyes straight in the all-important near-vision range, and their wearing often results in a remarkable improvement of the binocular cooperation. They must, however, not be prescribed at random, but on the basis of measurement, and they must be given in such a form that they are acceptable to the child and willingly used by him.

Extensive experience in the field of strabismus has shown the author that when a child with esotropia has been given glasses after a cycloplegic refraction and has worn them for some time, say a month, one of the following conditions will be found when the child is re-examined: (1) the angle of squint has been reduced to zero or almost zero both for distance and near fixation, and reasonably secure binocular cooperation may be present; (2) the angle of squint for distance has been removed or almost removed, but esotropia for near remains; (3) the angle of squint has been reduced but not eliminated for either distance or near fixation; or (4) the wearing of the spectacle correction has had no influence on the angle of squint for either distance or near fixation. In (1), the case is obviously one of pure accommodative esotropia, and the wearing of spectacles and possibly orthoptic treatment are all that will be required for a cure. In (4) the accommodative factor is of very little importance or altogether absent; surgery will doubtless be necessary, if warranted by the amount of deviation, and should be preceded and followed by orthoptic treatment as indicated. These two conditions need not be considered here. In (2) and (3), however, the wearing of glasses has produced a partial result, and these are the cases in which the effect of additional plus lenses on the angle of squint in near fixation should be investigated. This is best done by determining the angle of squint objectively with the prism and cover test, which is rapidly and easily performed, at least in the primary position, and requires a minimum of cooperation on the part of the patient. For the purpose under discussion, it gives the most reliable results.

In order to add plus lenses to the patient's glasses it is convenient to use an ordinary clip-on frame to which prongs have been added to hold the trial lenses;

the top bar connecting the two eyepieces should also be made adjustable so that the frame can be used with spectacles of different sizes. In this clip-on frame are first placed lenses of a power of plus 1.00 D sph. in front of each eye and the angle of squint is measured at a fixation distance of 33 cm. The amount of the angle is noted and the lenses are exchanged, increasing the power in steps of plus 0.50 D sph. up to plus 3.00 D sph., measuring the angle of squint with each change. Patients in whom no amount of additional plus power has a measurable effect on the angle of squint are obviously not candidates for bifocal glasses.

In other patients, a stepwise decrease of the angle of squint with each increase in the power of the added lenses will be noted until a point is reached at which the angle of squint is zero; further increase in power will then often reverse the condition and the patient will exhibit an exodeviation. Assuming that the addition of plus 2.00 D sph. before each eye has stopped the movement of redress in the alternate cover test, should bifocal glasses be prescribed? This depends on a number of factors. Bifocals are not ordered in the presence of an anomalous correspondence or of a significant amblyopia ex anopsia. But as soon as the retinal relationship has been normalized and the vision has been made to be substantially equal in the two eyes, the patient should be given bifocals, provided that the angle of squint for distance is minimal.

When bibocals have been decided on, a very large segment (28 mm. wide or more) with a straight top should be given, and it should be set higher than for the adult presbyope. The top of the bifocal segment should bisect the pupil when the child looks straight ahead. It is much easier for children to get used to bifocal glasses than it is for the average adult presbyope and so far none have had any difficulties with these bifocals. Parents occasionally question the use of bifocal glasses in children but as a rule they will accept them readily when told that the bifocals are not for permanent use, but are rather in the nature of an exercise. The length of time the bifocals should be worn depends on the development of the case and on the way in which it is handled. If the patient with accommodative esotropia develops fusion and amplitudes and is given orthoptic treatment, including exercises to dissociate convergence from accommodation, then the power of the lenses may be gradually reduced. But this, too, should only be done by measurement, always determining the minimum refractive correction which will keep the eyes properly aligned.

If the patients are proplerly selected and if the proper type of bifocal segment is ordered, the surgeon will be pleasantly surprised in most cases with the rapid development of binocular single vision and of fusional amplitudes. The author has seen many patients in whom bifocal glasses alone produced the sudden appearance of fusional amplitudes where previously there were none, or in whom they helped materially to establish increased amplitudes and more secure binocular cooperation.

Comment: Some of us have steered away from the prescription of bifocals, substituting the use of the miotic Floropryl for the following reasons. Not only do parents resent their children having to wear this type of glasses plus the increased expense involved, but we find that it is necessary to have orthoptic training to dissociate accommodation and convergence by building up the amplitudes of relative fusional divergence. This

necessitates the services of a skilled orthoptist, a child mature enough to benefit from such training, as well as a child with economic and geographic availability to take such training. Otherwise, although the bifocals might satisfactorily realign the eyes, conditions remain at a standstill in that without bifocals the eyes continue to cross.

PHILIP KNAPP

THE INTRAOCULAR PRESSURE

PRESSURE REGULATING EFFECT OF IRIDENCLEISIS

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Ophthalmologica, 1956, *132:* 48–56

Iridencleisis was performed with certain modifications of Holth's technique on 277 eyes with glaucoma at the ophthalmic clinic in Giessen, Germany, between 1951 and 1954. Gonioscopy was performed on 214 of these eyes before the operation and several times after surgery. A straight keratome incision was used (method 1) in 109 eyes, and with an *ab externo* separation of the sclera (method 2) in 105 eyes. The pressure was restored to normal in 89 eyes with the keratome incision, and in 102 eyes with an *ab externo* incision. Compensation was not achieved with method 1 in 20 eyes, and with method 2 in 3 eyes. In 11 of these 23 eyes a subsequent iridencleisis was successful, and postoperative normal pressure values were obtained finally in 202 (95 per cent) of the 214 eyes operated on. Twenty-two of the 202 eyes required instillation of miotics, and compensation did not occur in 12 eyes (5 per cent) only.

Five of the patients operated on were children between the ages of 6 months and 5 years with buphthalmus. The results obtained in these patients were excellent.

Visual function did not change in 179 eyes; function was improved in 19 eyes and became worse in 16 eyes.

Preoperative and postoperative examinations of the visual field showed that widening of the preoperatively limited field occurred in 13 eyes, particularly in the peripheral portion, and in 185 eyes the visual field was not changed. In 16 eyes the preoperative decrease of the visual field was aggravated. Temporary postoperative pressure oscillations with variable pressure values ranging from 15 to 35 mm. Hg occurred in 23 eyes and lasted for several weeks until the pressure was restored to normal without any further treatment.

Bacterial infections did not occur in any of the eyes immediately or later after the operation. Nonbacterial postoperative infections were considerably less important primarily than with cyclodialysis and Elliot's trephining.

The satisfactory results obtained are definitely in favor of method 2. It should be emphasized that with the aid of method 2 it was possible to obtain a fitting of the iris into the incision in most of the eyes. With this technique the iridencleisis was performed with the minimal amount of entry into the anterior chamber. The factors in successful regulation of pressure by iridencleisis procedures are the following: (1) the position of the draining slit, the ideal location for which is in the area between the scleral spur and Schlemm's canal; and (2) the width of the draining slit whose patency may be maintained in the most effcient manner by incarcerating the limb or the limbs of the iris in a fold.

Comment: At the present time there is considerable discussion as to which operative technique is likely to lead to the greatest success with the iridencleisis operation. Not only are the *ab externo* versus keratome incision debated but the efficacy of the anterior or posterior sclerotomy and the anterior flap sclerotomy and one versus two-pillar incarceration is under discussion. From a theoretic viewpoint it certainly is true that pressure by the scleral lips tends to close the scleral drainage channel. Jamming the pillar or pillars in one or both edges of the incision may be better than allowing the everted iris to be flat between the wound edges. Sclerotomy, especially of the anterior type, also tends to enhance drainage. As has been learned during the history of the use of iridectomy for acute angle-closure glaucoma, an *ab externo* incision tends to be more ragged, a little greater in width and, therefore, more efficacious. This fits in with the findings of Vilmar.

One should consider the actual location of the incision. Vilmar feels that the best location is in the area between Schlemm's canal and the scleral spur. Van Beuningen considered the ideal location to lie between Schlemm's canal and Schwalbe's ring. Others feel that it is important that the inner end of the incision should go through Descemet's membrane. In using a keratome there is a longer tract through the sclera-cornea since the incision is always away from the perpendicular. The intraocular pressure tends to close the incision as if it were a valve. With an *ab externo* approach, the incision can be perpendicular to the cornea as with the Weeker's operation and is, therefore, shorter. Pressure from within would not tend to close the wound but rather to open it. It is obvious that there is no unanimity of opinion as to the factors involved in the success of iridencleisis. Suffice it to say that the *ab externo*, perpendicular incision probably is to be preferred to the keratome incision.

H. Saul Sugar

ON THE FRONTAL AND DIENCEPHALIC CENTER AS A REGULATOR IN GLAUCOMA

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Arch. d'Opht., 1956, *16:* 507–530

The need for frontal surgical operations in patients with primary glaucoma and psychic syndromes gave the author an opportunity to investigate the possibility that there is in the frontal region of the brain a regulatory center governing

intraocular pressure. All the clinical forms of primary glaucoma, with some cases of congenital hydrophthalmos, were included in the study, but secondary glaucoma was, of course, excluded.

The pneumoencephalographic findings in 21 patients, 6 of whom had acute or chronic congestive glaucoma, 8 simple glaucoma, 4 congenital hydrophthalmos, 2 Sturge-Weber syndrome, and 1 Marfan's syndrome with hydrophthalmos of the right eye, disclosed the existence of cortico-subcortical atrophy of the frontal part of the brain and, in 8 cases, of frontoparietal atrophy. The ventricular system was enlarged in 12 cases, indicating the presence of internal hydrocephalus; in addition, the chiasmatic cistern showed dilatation in 10 cases and the interpeduncular cistern, in 5 cases. Diencephalic-mesencephalic atrophy was present in addition to the cortical frontoparietal atrophy.

The results of the Pandy test were positive in 14 of the 21 patients. Positive audiographic findings, strongly suggestive of a bilateral lesion of the acoustic nerve, were obtained in six patients. Moreover, symptoms indicative of chronic encephalitis were also discernible.

The intraocular pressure, the brachial artery pressure, and the retinal pressure in relation to the ophthalmic arteries, were determined before and after operation in five patients subjected to bilateral transfrontal lobotomy and one who underwent a unilateral frontal lobectomy. The data obtained by these determinations argued in favor of a regulatory center governing intraocular pressure and blood pressure in the frontal part of the brain: a synchronous rise or fall in these pressures was frequently observed.

These findings, taken as a whole, support the author's theory of the origin of primary glaucoma, according to which the condition begins with an inflammation or intoxication leading to cerebral atrophy in the diencephalic-frontal part of the brain, primarily throughout the whole neurovegetative region, with symptoms resulting from cerebrovegetative dysfunction. This dysfunction, in turn, finally manifests itself in the eye in the form of glaucoma.

INTRAOCULAR PRESSURE REGULATING-CENTER IN FRONTAL PORTION OF BRAIN IN PATIENTS WITH PRIMARY GLAUCOMA

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Ophthalmologica, 1956, *132:* 76–86

In nine patients between the ages of 17 and 40 years with schizophrenia, intraocular pressure and blood pressure recordings were made two to three months after the patients underwent transorbital or transfrontal prefrontal lobotomy or lobectomy. In four of the nine patients the intraocular pressure showed slight oscillations, in three patients the intraocular pressure dropped, and in two pa-

tients it was increased. Slight oscillations of the blood pressure were observed in two patients; lowering of blood pressure occurred in six, and rise of blood pressure in one. A synchronous lowering of intraocular and of blood pressure apparently occurred in two patients, and a synchronous rise in one. All these pressure oscillations were considered as direct sequelae of the operative trauma in the frontal areas of the brain.

Encephalographic studies were carried out in four patients between the ages of 6 and 55 years with glaucoma. Encephalographic findings in all the patients were positive in the sense of atrophic cerebral changes in the frontal or parieto-occipital segments. Two of these patients had glaucoma simplex, one had chronic congestive glaucoma, and one had monolateral buphthalmus. These observations induced the author to assume that there is a relationship between the changes in the brain and the glaucoma and that there may be situated in the frontal area of the brain a center which exerts a regulating influence on the intraocular pressure and on the blood pressure. It seems probable that this cerebrofrontal center is connected by an intimate common function with the diencephalic centers which are regulating the intraocular and blood pressures.

Comment: The subject of an intraocular pressure regulating center is always intriguing but lends itself to much speculation. Most of the experimental work points to a diencephalic center rather than to a frontal one, although Čavka considers the cerebrofrontal center to be intimately connected with the diencephalic centers.

The synchronous relation of the blood pressure to the intraocular pressure in these cases may be of considerable importance. Von Sallmann and his co-workers (Am. J. Ophth. 1956, *42:* 130) showed that stimulation of the ventral hypothalamus caused a rapid rise in intraocular pressure which was subordinate to the coexisting elevation of systemic blood pressure. When the influence of increased blood pressure was annulled, the intraocular pressure failed to react to central stimulation.

It is important to point out that the relation between the positive encephalographic findings and the presence of the various types of glaucoma must be considered with considerable care. First of all, our clinical experience indicates that hydrophthalmia is a purely ocular condition unless related to angiomatosis in which case one could understand a positive encephalogram. There have been no similar corroborative findings of encephalographic changes in glaucoma which would give the remaining 3 cases significance.

SAUL SUGAR

NEUROLOGY

ARTERIOVENOUS FISTULA IN CAVERNOUS SINUS (PULSATING EXOPHTHALMOS SYNDROME)

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Klin. Monatsbl. f. Augenheilk., 1956, *128:* 641–657

The term arteriovenous fistula rather than arteriovenous aneurysm is suggested for the acquired or traumatic communication between the cavernous sinus and the internal carotid artery which caused a pulsating exophthalmos syndrome in seven patients described. The rupture of the carotid artery was caused by severe injuries to the skull in five patients. One patient had sustained a fracture of the base and a fracture of the sella seemed likely. In one patient, the pulsating ophthalmos syndrome occurred in the right eye after injury of the left eye by a rod which was pushed accidentally in the left eye of the patient causing rupture of this globe.

The pulsating exophthalmos syndrome is the clinical manifestation of the short-circuit in the carotid "siphon". Varicose dilatation of the superior ophthalmic vein results and is associated with a pulsation which affects the entire eyeball. Only after an interval up to several months after the injury did several of the patients complain of unilateral headache and of pain behind the eye. A sound described as rumbling was heard and protrusion of the eye was observed in the mirror. Neurologic examination revealed lesions of the oculomotor nerve and an increasing diminution of visual function approaching blindness. More or less pronounced disturbances of the trochlear nerve were observed, and the abducens nerve was frequently impaired. Characteristic pressure phenomena involving the trigeminal nerve resulted in painful signs of irritation or deficiency in the area of distribution of the upper two branches which occasionally caused symptoms similar to "migraine". In all patients a blowing murmur could be heard over the temple and the mastoid process on the side of the fistula. This symptom disappeared as soon as the common carotid artery was compressed on the affected side. In one patient with a crossed exophthalmos this symptom disappeared when the contralateral common carotid artery was compressed.

Serial arteriograms and pneumoencephalograms proved valuable for the demonstration of the functional and anatomic conditions. The size, the location and the flow of the arteriovenous fistula was established with the aid of the arteriography, while damage to the substance of the brain caused by the fistula was determined with the aid of the pneumoencephalogram.

The agonizing vascular sound and the deterioration of vision require early treatment. The ideal aim of vascular surgery is the restoration of the original

circulation, but this is not possible for anatomic and technical reasons. The scar formation which occurs after direct injuries most often prohibits a palliative intracranial intervention in the form of vascular ligation or muscle tamponade. As a rule extracranial ligation of the arterial inflow or the venous outflow is advocated. Ligation of the orbital veins anteriorly or laterally seems to be more promising. The purpose of this method of treatment is the artificial production of an ascending thrombosis which causes occlusion of the arteriovenous fistula. Interruption of the common carotid artery and of the internal carotid artery, respectively, in the area of the neck have the purpose of producing a thrombus in the fistula or at the point of perforation of the artery.

In one of the authors' patients, a 14-year-old boy, a conservative method of treatment devised by Clausen was employed successfully. Compression of the carotid artery was attempted with a covered gramophone spring which was placed around the neck similar to a truss, and one end of the spring was reinforced by a felt pad (pelotte) shaped like a cone. This pad was placed on the vascular bundle on the neck. The visual function of the eye was restored to normal and the syndrome disappeared after nine and a half months. Cures were also obtained in the six other patients. Thrombosis of the fistula was produced by the pelotte method in a second patient, a 64-year-old woman. In three other patients ligation of the common carotid artery was performed; ligation of the cervical portion of the internal carotid artery was done in one patient and ligation of the common carotid and external carotid arteries in another.

In one of the patients, a 64-year-old man, with severe fracture of the skull and traumatic blindness of the right eye, the ligature of the common carotid artery restored the much reduced vision on the left pulsating exophthalmos side close to normal. These results showed that treatment of pulsating exophthalmos must not always be an active-surgical one, but that excellent results may be obtained with conservative methods.

Comment: The interested reader will find an excellent paper by Walker and Allègre (Surgery 1956, *39:* 411) on this same subject. A greater number of cases (24) was reported, with a ratio of 14 traumatic to 10 spontaneous fistulas. The spontaneous cases are more frequent in women, with pregnancy a precipitating factor in about one-fourth, suggesting the rupture of a preexistent aneurysm in the cavernous sinus.

To the classical signs of unilateral (or rarely bilateral) exophthalmos, pulsation of the eyeball, and a bruit audible to both patient and physician, should be added the characteristic venous injection and chemosis which is present in many cases. One series reported 159 cases with chemosis in 224 collected instances. Visual disturbances were present in only 66 of the 224 cases. Diplopia was present in about a third of the cases, and was usually due to sixth nerve involvement.

In their cases, Walker and Allègre found blindness in the affected eye in almost one third of the patients, with some loss of vision in practically half the individuals. Their treatment results showed that the "trapping" operation where cervical ligation of the internal carotid artery was used with intra-cranial clipping to isolate the fistula relieved the pulsating exophthalmos more consistently than simple ligation of the carotid. However, serious complications may follow either method.

It should be remembered that a stab wound of the orbit which appears minor at first glance can lead to a carotid-cavernous fistula. One such case seen in our clinic had been stabbed with an ice pick through the upper lid, with a minor wound in the skin. Pulsating exophthalmos developed during the next 24 hours. At autopsy, the tract of the ice pick extended well into the brain stem, having passed through the superior orbital fissure, carotid, and cavernous sinus.

JOHN WOODWORTH HENDERSON
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NEURO-OPHTHALMOLOGIC EXAMINATION OF CHILDREN

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Neurology, 1956, *6:* 739–743

The neuro-ophthalmologic examination of children presents difficulties similar to those encountered in any examination in which cooperation from the patient is necessary. It is no harder to examine a cooperative child than it is to examine a cooperative adult, and an uncooperative individual is difficult or impossible to examine at any age. In testing the eyes of children, there is sometimes a temptation to be less persistent or thorough than with adults, but actually a higher degree of effort and skill is required to obtain the information that is needed.

In a neuro-opthalmologic examination, the following observations must be made: (1) visual acuity, (2) pupillary condition and reactions, (3) symmetry, parallelism, and movements of the eyes and eyelids, (4) ophthalmoscopy, and (5) visual field examination.

(1) In testing the vision of infants, the examiner should note the pupillary light reaction, whether blinking occurs in response to a bright light, and also whether the child fixates and follows a bright object. It is important to have an approximate knowledge of the patient's visual acuity. This may be obtained by the aid of marbles in children under three. If a marble of 1½-inch diameter is recognized at 20 feet, this indicates a visual acuity of 20/200; a- ¾inch marble recognized at 20 feet indicates 20/80 vision. Children aged 4 to 6 cooperate well enough as a rule to permit the use of the E chart; the large plastic E held in the hand is often very useful. Once a child is familiar with the names of letters, he is usually very easy to test because of his eagerness to demonstrate his knowledge of the test letters.

(2) The pupils of premature infants do not react well, and they are also hard to dilate widely. Full-term infants, however, have good pupillary reactions. Slight pupillary inequality may be present up to the age of 3 or 4 years.

(3) Ocular deviations are often very difficult to diagnose when the child is 4 years old or less. Testing the ocular rotations requires a certain degree of cooperation. A small but nevertheless important amount of strabismus may easily be overlooked. The most valuable procedure in children of any age is to watch the eyes move as they follow the examiner's finger. The next most important is to employ the cover test, observing the ocular movements (1) at the time one eye or the other is being occluded, and (2) when the occluder is being removed. The horizontal ocular muscles should be tested by having the child move the eyes first to one side and then to the other, but the vertical muscles should be tested only by having the child move the eyes up and down from the position of far right lateral gaze or far left lateral gaze. The presence of an epicanthus or facial asymmetry should not mislead the examiner, since the alternating cover test will corroborate or dispel the impression of an ocular muscle abnormality. Nystagmus in children differs in no way from nystagmus in adults, except for the rarely observed nystagmus nutans, in which an infant of less than three months of age develops nystagmus and head-nodding. Irregular wandering movements of the eyes can sometimes be seen in infants and children with very poor vision.

(4) Infants up to the age of about 6 months can usually be examined ophthalmoscopically quite easily without anesthesia, using 2 per cent homatropine drops for dilating the pupil. Important lesions are sometimes encountered in the peripheries of the fundi and so, if these areas cannot be seen, the examination should be repeated using rectally administered pentothal sodium as an anesthetic. Most children 5 years of age or more can cooperate sufficiently for ophthalmoscopic examination. Children up to the age of 5 can be examined most advantageously while they are lying down. The cornea, iris, and vitreous should also be explored with the plus 6 or plus 8 lens of the instrument, since many lesions may be easily overlooked when the examiner is eager to see the fundus and optic disk. The ocular fundi of young children are somewhat different from those of adults, because development of the choroidal and retinal pigment and of the macula is still incomplete at birth. Children up to the age of about 3 years have pale disks, and it is often difficult to decide whether the pallor is pathologic or normal. The three major pitfalls to be guarded against in interpreting the infant's fundus are (1) an erroneous diagnosis of optic atrophy because of the gray color of the disk, (2) misinterpretation of the grayish color of the undeveloped macula, leading to a false diagnosis of macular degeneration or even of tumor, and (3) misinterpretation of the grayish peripheries of the retina as glioma, degeneration of the retina, or retrolental fibroplasia. The problem of correct diagnosis of elevated optic disks is complicated by the existence of many congenital variants. True papilledema may be due to increased intracranial pressure (so-called choked disk), hypertension, septic conditions, increased protein in the spinal fluid, optic neuritis, orbital lesions, and other causes. These can almost invariably be differentiated by ophthalmologic examination alone.

(5) The visual fields cannot be tested very reliably in children younger than 7 or 8 years old, because so much depends on subjective findings. An occasional child of 6 may give satisfactory cooperation, but most children must be 8 years

of age or older before their visual field defects have localizing value. Findings of relatively reliable lateralizing value, however, may be obtained by gross examination of the visual fields of children even six months old or less.

Comment: This concise article is an excellent review of the techniques and importance of neuro-opthalmic examination in infants and children. An additional point in the diagnosis of possible abducens palsy in young children is the use of total occlusion with an Glastoplast occluder in the occasional patient who prefers to cross-fix rather than abduct either eye. This should be done on each eye in turn for several days at least in order to assess adequately the possibility of lateral rectus palsy.

Mentioned in the original article is also a word of warning to those who would be likely to diagnose an abducens palsy in a child who has a Duane retraction syndrome. The usual differential points of retraction of the inner canthus, closure of the lids on adduction and the like are mentioned by the author.

A further help in the fundus and external examination of infants is the timing of the visit so that the child is ready for his next bottle feeding at the time of examination. In our clinic a bottle warmer is standard equipment to facilitate such examination. In other cases, a sterile rubber nipple may be used as a similar strategem.

I believe strongly in the principle elicited in the original paper of having the patient return for several short visits rather than going beyond the child's attention span with a prolonged first visit. This is especially true of retarded children who may be quite difficult to manage at the first visit, but who can be examined completely if the office visits are made a happy occasion.

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THE ORBIT

LESIONS OF THE OPTIC NERVE IN EXOPHTHALMOS OF ENDOCRINE ORIGIN

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Am. J. M. Sci., 1956, *232:* 226–239

In most cases of exophthalmos of endocrine origin, the balance between the thyroid hormone and the thyrotropic hormone of the pituitary is disturbed. Yet there are cases in which no disturbance such as an excess of pituitary thyrotropic hormone can be demonstrated, and this suggests the existence of an exophthalmos-producing substance distinct from the thyroid-stimulating hormone. Animal experiments and other evidence recently obtained also tend to show that there are two separate factors, one being responsible for the exophthalmos and the other exerting a stimulating action on the thyroid gland. Indications are that the exophthalmos-producing factor in pituitary extracts is much more closely associated with the thyrotropic hormone than with any other single principle, including corticotropin and the growth hormone.

In most patients with thyrotoxicosis, exophthalmos if present is not materially progressive; in some, however, progressive exophthalmos (malignant exophthalmos, exophthalmic ophthalmoplegia) may lead to visual loss as a result of injury to the optic nerve. Severe progressive exophthalmos has also been found in patients euthyroid after thyroidectomy and even in persons with no evidence of past or present thyrotoxicosis. Whatever the nature of the endocrine imbalances accompanying exophthalmos, local tissue changes in the orbit seem to be the one common factor capable of affecting the optic nerve. Orbital changes in patients with exophthalmic goiter of the usual type consist of widespread neuromuscular degeneration, occasional infiltration of round cells, fat infiltration, and some fibrous replacement in the disintegrating muscle and nerve cells. In patients with malignant exophthalmos, on the other hand, the changes include pronounced enlargement of the orbital muscles, edema, varying degrees of cellular infiltration, and phagocytosis of fat. One of the most characteristic distinguishing features of progressive exophthalmos seems to be an increase in intraorbital tension. In cases of nonprogressive exophthalmos, the globe can be pushed back into the orbit by firm gentle pressure; in cases of progressive exophthalmos, on the other hand, the definite retrobulbar resistance encountered makes replacement impossible. Orbitonometry provides accurate measurements of the resistance to backward pressure, so that its increase can be followed.

Detailed quantitative studies of orbital tissues removed from one patient with malignant exophthalmos and from control subjects, some without exoph-

thalmos and some with thyrotoxicosis with exophthalmos, led Rundle, Finlay-Jones, and Noad to conclude that the critical factor in exophthalmos is the ratio between orbital tissue bulk and orbital volume. The association of bulged lids, epiphora, and chemosis had led to the erroneous assumption of widespread orbital edema. Edema of the orbital contents may, however, be a terminal development when extreme degrees of overfilling cause obstruction of the orbital veins.

The vision in cases of exophthalmic ophthalmoplegia remains unimpaired unless complications develop. These, unfortunately, are frequent and include exposure keratitis, which may end in endophthalmitis and loss of the eye, and papilledema resulting in optic atrophy. Retrobulbar neuritis is a rare complication. Generally speaking, hyperthyroidism is not accompanied by ophthalmoscopically visible changes, although optic neuritis has been reported in some cases. The visual loss which appears in the late stages of progressive exophthalmos may be due to a variety of causes. Drying of the cornea may cause blurring, but the more serious losses are caused by corneal ulceration, choked disks, and changes in the visual fields, which may vary from slight peripheral constriction and enlargement of the blind spot to marked irregular loss of field. Reduction of visual acuity caused by choked disks with retinal hemorrhages occurred in 17.5 per cent of one series and blurring of the disks was present in a larger number. Attention has been called to the fact that the so-called papilledema accompanying exophthalmos is not due to increased intracranial pressure; rather, it seems to be actually an edema of the retina proper. Scotomas of various sizes may be present in various parts of the visual fields of patients in whom exophthalmos is associated with considerable retro-orbital resistance. They may involve only quadrants or the entire lower or upper half of the visual field, and they may become large enough to cause virtual blindness. More than one authority can be cited to show that nonspecific field changes and marked diminution of visual acuity may occur in the more severe cases of progressive exophthalmos.

Progressive exophthalmos and glaucoma are sometimes associated. In some cases, the increase in intraocular tension is apparently due to the increased intraorbital pressure. Control of the exophthalmos is usually accompanied by improvement in the glaucoma. Vision, though sometimes lost or severely impaired, has been known to return to normal as the pressure declined. Edema of the disks accompanying progressive exophthalmos was associated with a definite reduction in vision in 16 out of 18 cases. The various diagnoses made by the observers in these cases were papillitis (6), retrobulbar neuritis, optic neuritis, and choked disk (1 each), papilledema (6), and, simply, edema of the disks (3). Whether the edema of the disk is caused by compression of the nerve by orbital edema, whether it indicates increased intracranial pressure, or whether it represents optic neuritis, is not known. If intraorbital hypertension is relieved in time, the outcome is usually favorable, but there are cases in which optic nerve involvement ends in optic atrophy.

The most frequent type of optic nerve involvement in malignant exophthalmos was said by Offret and Offret to be retrobulbar neuritis, characterized by progressive failure of vision with central scotoma and without fundus lesion. Normal

vision was regained in 9 of 13 cases with retrobulbar neuritis collected from the literature. Apparently, the prognosis for vision is better in cases without ophthalmoscopically visible changes in the optic disks than in cases with such changes.

The lesions of the optic nerve in patients with malignant exophthalmos are poorly understood, but microscopic examination in one case showed marked atrophy of the muscles and optic nerve with fibrous and fatty areolar connective tissue replacement. Compression of the trunk of the optic nerve is known to be capable of causing foci of segmental degeneration, but since vision sometimes improves after orbital decompression, degeneration cannot have been the cause of the initial loss of vision. The question arises whether simple compression or edema may be the primary cause of the loss of vision. Even agreeing that compression may produce foci of degeneration in the optic nerve, it can still be argued that complete functional recovery may be attained if the compression is removed soon enough.

Opinions differ somewhat as to the mechanism by which the optic nerve lesions are caused. Some attribute them to stretching of the nerve; others, to the increase in orbital pressure leading to pressure on the nerve and impairment of its circulation. Still another explanation is that pressure changes may occur in the optic nerve when there is marked orbital edema, leading to swelling of the lids and infraorbital tissues. If, on the other hand, as Mulvany suggests, the edema of the lids and conjunctiva is due to obstruction of the palpebral veins and not to waterlogging of the retrobulbar tissues, a good recovery may be expected if the pressure is relieved before vision has failed completely.

Many different forms of treatment have been tried in progressive exophthalmos. Efforts have been made to prevent the conversion of benign into progressive exophthalmos, but the results of medical therapy are hard to evaluate because many patients recover spontaneously and many others are treated only when the exophthalmos has reached an irreversible state. Involvement of the optic nerve is generally agreed to be an indication for surgical decompression. This procedure, though only palliative, is apparently the best means available at present for the protection of the cornea and the optic nerve until the disease has run its natural course. To obtain the best results, the operation should be performed as soon as possible after the appearance of evidence indicating optic nerve involvement, and it should include removal of the lateral wall of the orbit as well as of the orbital roof.

Comment: This article offers one of the most complete reviews on this particular phase of endocrine exopthalmos that has appeared in either the ophthalmic literature or textbooks of ophthalmology. In addition to his discussion of the types, behavior, pathogenesis, and treatment of the optic nerve lesions, the author has summarized the opinions as to the pathologic changes that occur in the orbit in this puzzling type of exophthalmos. In a sense, the article is a condensation of the more important publications that have appeared in the already voluminous literature on the ophthalmic aspects of Graves' disease and does not lend itself well to either further condensation or review.

In brief, the lesions that affect the optic nerve are (1) those accompanying a glaucoma which, in turn, seem to be secondary to the changes in the orbit; (2) a disorder which re-

sembles retrobulbar neuritis in its behavior; and (3) a disturbance at the optic papilla which may or may not be accompanied by loss of vision. All of these disturbances of the optic nerve are considered to be a complication of the severer forms of endocrine exophthalmos. Beyond this point the subject becomes a mass of confusion and mixed opinions.

Part of this confusion can be attributed to the terminology that is used by the various authors in their descriptions of individual cases. The term "choked disc" is used by some to describe a change in the optic papilla that by others has been designated a papilledema. The terms "papillitis" and "optic neuritis" seem to have different connotations to different writers.

Another source of confusion is the tendency of clinicians to report only one or two cases of these optic nerve complications and then attempt to draw conclusions on the basis of such a brief survey. In some of these "single" case reports the period of observation is so short as to preclude an opinion as to the final outcome of the disturbance in the optic nerve. In this respect, this reviewer realizes that these optic nerve lesions are not common and the opportunity to see a large number of these cases is a privilege of only a few opthalmologists working in larger centers.

In many instances, however, the correct nature of these complications in the optic nerve are not recognized by the casual observer because an examination of the visual field is not performed in suspected cases. In these situations the observer by a process of exclusion points the finger of suspicion toward the optic nerve as the locale for the visual loss, but, unfortunately, visual fields are not documented to prove this point.

The majority of the observers cited in the text are of the opinion that the disturbances of the optic nerve in endocrine exophthalmos are secondary to the increased intraorbital tension, or, increased bulk of the tissues in the posterior portion of the orbit. It is my feeling that such factors are responsible for the secondary glaucoma and the papilledema unaccompanied by visual loss that are listed as complications. However, I do not feel that such "mechanical" factors are responsible for the retrobulbar type of disturbance and the papillitis accompanied by immediate diminution of vision. I would favor either some neurotoxic or vasospastic disturbance in the optic nerve as a possible explanation for these latter complications.

The reader is cautioned to maintain a very objective viewpoint when it comes to interpreting the beneficial effects of any given treatment on these complications of endocrine exophthalmos. Particularly is this viewpoint needed when the results of orbital decompression are considered. Most of the writers cited by the author had noted the disturbance in the optic nerve in the later stages or more severe types of malignant exophthalmos. Therefore, to relieve the threat to vision by reason of the disturbance in the optic nerve, decompression was advised and in those cases wherein there was a subsequent improvement of vision the act of decompression received the credit. I agree that it would require a brave clinician to advise against such heroics in the presence of visual failure. However, those cases wherein the vision became worse following a decompression operation are seldom reported, and in my own experience the "retrobulbar" and "papillitis with early loss of vision" types of cases may improve without this surgical procedure. On the other hand, the "glaucoma" and the "papilledema with enlarged blind spots" types of cases are probably best managed by early surgical decompression of the orbit.

Although the above publication is complete in most all details, I regret that Dr. Wagener did not intersperse more of his own comments and opinions relative to the behavior of these disturbances of the optic nerve.

JOHN W. HENDERSON

THE RETINA AND VITREOUS

SPONTANEOUS REGRESSION OF RETINOBLASTOMA

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Brit. J. Ophth., 1956, *40:* 449–461

The records of the Children's Tumour Registry of the Departments of Child Health and Pathology, Manchester University, show that 165 tumors were found in children under 15 years of age living in a region containing about one million children during the two years ending September 1, 1955; of these 8 were retinoblastomas. Only two of the eight patients with retinoblastoma had a family history of the disease; these two were brothers, and evidence was obtained to show that their father had suffered in infancy from bilateral retinoblastoma which regressed spontaneously. The pedigree of the family, which was the subject of two earlier reports in the literature and which was cited by Griffith and Sorsby (1944), has now been brought up to date. It shows that the disease apparently started in the paternal grandmother, who had only one eye affected. The other members of the family who inherited the disease had bilateral growths. The family tree indicates that the predisposition to retinoblastoma was inherited as a dominant characteristic, the grandmother being heterozygous in that respect. The noxious gene was passed on to five of her children, but almost certainly missed one of her daughters, who has five surviving unaffected children. Whether her one son was also missed is not certainly known since he has only one child. In interpreting the inheritance in this family, the experience of Falls and Neel (1951) is relevant. They showed that members of a retinoblastomatous family, even though their fundi are normal, may pass the disease on to their children.

In addition to the retinoblastomas found in the eyes of the two brothers, ocular abnormalities were apparent in the eyes of three other surviving descendants, all of whom were examined by the authors. One, a boy aged 9 years, has a right marginal lens coloboma; the second, a man aged 38, has a left total cataract said to have been present for many years; and the third, the father of the two brothers, aged 37, whose history of ocular abnormalities dates back to infancy, had phthisis bulbi of the right eye; vision in the left eye was 6/60 and the fundus showed a large clear-cut area of chorioretinal atrophy. As the right eye was useless and unsightly, it was enucleated and examined histopathologically. The center of the globe was occupied by scattered clumps of calcified tumor cells, in which the individual cell elements were clearly recognizable.

In the 15 cases of spontaneous regression of retinoblastoma contained in the literature in which the evidence both for the diagnosis and for the regression was

satisfactory, the diagnosis has been based on four types of evidence: (1) a family history of the disease; (2) a clinical diagnosis of bilateral retinoblastoma with removal of one eye only (usually with histologic proof), followed by arrest of the growth in the other; (3) a fundus picture corresponding to that of verified cases; and (4) calcified tumor cells in phthisical eyes.

Three main elements can be recognized in the fundus appearances: (1) discolored raised areas in the retina, sometimes showing a lobulated or map-like pattern; (2) chalky-white patches indicative of calcification; and (3) areas of chorioretinal atrophy, usually forming a background for the tumor remains. These three elements may be superimposed or separate. Thus it is necessary to envisage the possibility that certain of these neoplasms, even of considerable size, may heal, leaving a clinical picture indistinguishable from a patch of old choroiditis. However, the disappearance of retinal vessels over part of their course, and their emergence, apparently *de novo*, in the middle of an atrophic area seems to be peculiar to healed retinoblastoma.

Since the arrest of the growth may occur in both eyes, it is unlikely to be due merely to accidental ischemia or reactive inflammation. In some cases of spontaneous regression phthisis bulbi resulted, while in others some sight was preserved without shrinkage of the eye. The father of the two brothers seems to be the first patient to be reported in whom bilateral regression had led to one phthisical and one sighted eye. Assuming the same mechanism in both eyes, the final result must be related to the degree of ocular disorganization at the time of arrest; it is unlikely that the destruction of the tumor is secondary to the phthisis bulbi.

In each of the two brothers, the right eye was enucleated and the left eye was treated with diathermy, and in one, with radon.

DIFFICULTIES IN THE CLINICAL DIAGNOSIS OF RETINOBLASTOMA

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Ophthalmologica, 1956, *132:* 162–164

Anatomic examination of 15 eyes enucleated for suspected retinoblastoma during the last five years showed retinoblastoma to be actually present in 8. Two of the remaining 7 showed the cicatricial stage of retrolental fibroplasia, two showed a retinal detachment, one an angiomatosis of the retina, one a microphthalmos with choroidal coloboma, and one an anterior synechia of the lens with congenital (?) cataract. The cause of the retinal detachment in the two

cases could not be established; in one of these eyes, however, a retinal tear was observed that may have been traumatic in origin.

In spite of the diagnostic error of nearly 50 per cent found in these cases, it must not be assumed that ophthalmologists are too readily inclined to enucleate an eye in which retinoblastoma is suspected. This is definitely not true. In many cases, the above-mentioned erroneous diagnoses were established after an examination under general anesthesia by two skilled ophthalmologists. Enucleation is indicated in all questionable cases, especially when the visual function of the eye is lost. In this connection the case of a child aged 1½ years, admitted to hospital with suspected retinoblastoma is illuminating. Examination under general anesthesia by two ophthalmologists could not definitely confirm the diagnosis. The child was discharged, but returned within a month to the outpatient department with metastases of retinoblastoma in the iris. Anatomic examination confirmed the diagnosis.

The only exception to the rule that all eyes in which retinoblastoma is suspected should be treated as if retinoblastoma were known to be present is to be found in patients with microphthalmos. Reese has stated that retinoblastoma never gives rise to the development of microphthalmos.

Comment: The author appears quite surprised by the diagnostic error of nearly 50 per cent in his series of 15 eyes enucleated for suspected retinoblastoma. It is doubtful, however, if this percentage, which seems to be approximately the same in ocular laboratories with a large volume of histopathologic material, will ever be lowered appreciably, without transgressing over the safety margin.

With the exception, perhaps, of retrolental fibroplasia, where careful study of the other eye should yield valuable diagnostic information, the conditions, usually misdiagnosed as retinoblastoma such as massive retinal separation in infancy, advanced retinal angiomatosis, parasitic retinal detachment, etc., cannot be definitely recognized clinically. It is safer to remove such eyes, many of which become troublesome in later life, with a secondary glaucoma and as a locus minoris resistentiae.

BERTHA A. KLIEN

DIFFERENTIAL DIAGNOSIS OF DARK LESIONS OF THE POSTERIOR FUNDUS

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Trans. Pacific Coast Oto-Ophth Soc., 1955, *36:* 87–97

The clinical problem of the diagnosis and management of small dark lesions of the posterior fundus is a difficult one. A dark lesion of the posterior fundus may be a melanoma, either benign (nevus), or malignant, a subretinal hemorrhage,

a disciform macular degeneration, an inflammatory lesion, a hemangioma, or a metastatic lesion.

It is well known that hemorrhage behind the retina may be the first sign of disciform degeneration. Such a hemorrhage presents as a localized, dark, elevated mass and looks precisely like a melanoma. A nevus may appear slightly elevated, dark, and localized, and may occasionally be confused with a melanoma. A melanoma itself may or may not be very elevated, may vary in color from very light to all shades of darkness, and the pigment may be unevenly distributed, as usually seen in chorioretinitis. A hemangioma is elevated, localized and may be darker than the surrounding fundus. Inflammatory lesions may also appear as localized dark masses.

On ophthalmoscopic examination all these lesions are dark. The pigment is so conspicuous that it tends to dominate the clinical picture, but pigmentation contributes little to the diagnosis or prognosis. The "blue ointment" appearance of choroidal nevi is usually characteristic, but even in this instance the pigmentation can be misleading since these lesions can become darker or lighter without reference to malignant change.

The location of the lesion is of some help in the differential diagnosis. Disciform degeneration occurs only in the macular region but it may be eccentric in relation to the fovea. Melanomas may arise anywhere, but those in the macula must be regarded with suspicion as the possibility of disciform degeneration is so great in this region.

The size of the lesion is of no aid in the diagnosis, but the rate of increase in size is. A marked increase in size within a few days speaks against a tumor and is more characteristic of a disciform lesion associated with hemorrhage or serous fluid. Increase in size associated with increasing blurring of the lesion is in favor of inflammation. A tumor tends to become more distinct as it becomes larger.

If the dark lesion is associated with hemorrhage, then the weight of evidence is overwhelmingly against melanoma. Generally hemorrhage occurs with larger or necrotic melanomas or ones that have broken through Bruch's Membrane. Small melanomas of the posterior pole are so rarely associated with hemorrhage that the eye should not be enucleated unless there is some other unusual reason for enucleation. Grossly visible subretinal hemorrhage is frequently found with disciform macular degeneration.

Occasionally a hemorrhage below the retina or in the choroid will appear only as a dark globular mass which transilluminates poorly. If such a lesion does not show a slight redness in one area suggesting blood by ophthalmoscopic examination, it will usually show this on slit-lamp and contact-lens examination. If the slit-lamp beam is directed slightly to one side of the lesion, a slight pink or reddish halo may be seen at the edge of the lesion. Absence of new blood vessels deep to the retina in the latter may make one suspect that a melanoma is not present. If one remains in doubt, time, drawings, and fundus photography may provide a more satisfactory answer than histologic examination. With the passage of time, such an elevated localized dark lesion gradually transforms into the characteristic elevated white lesion of disciform degeneration.

Traction folds, whether radial or concentric, are frequent in inflammatory

lesions, especially when fresh. The concentric folds may be found with angiospastic retinopathy, central serous retinopathy, or edema of the retina. Traction folds of any type are rare with tumor and are definitely against this diagnosis.

A retinal detachment associated with a dark lesion of the posterior pole is the sign par excellence of a melanoma. The elevated retina tends to be smooth, with little tendency to wrinkle, and usually without a break. Difficulties in diagnosis occur if the detachment is so extensive and the retina so elevated that no indication of a tumor is present. If the detachment does not reach the periphery, or no break in the retina is present, one should be suspicious and a proper period of bed rest with binocular pads may reveal the diagnosis.

The retinal separation may be so slight that it is overlooked without careful slit-lamp examination, or it may be so far in the periphery and so slightly elevated that it is overlooked without careful field studies. The significance of a retinal detachment with a dark lesion is the same whether the detachment is extensive or minimal, central or peripheral—it means that the lesion is very probably a melanoma. In occasional cases a slight elevation of the retina may be seen adjoining a disciform lesion if the lesion is examined by slit-lamp microscopy.

Others signs on ophthalmoscopic examination which are of occasional aid are presence of a light fringe or marginal pigment disturbance which speaks against a nevus, vitreous opacities which draw attention to an inflammation, and drusen. These excresences of the lamina vitrea are consistent with a melanoma but can occur with any chronic disturbance of this glossy membrane.

Examination of a fundus lesion is not complete without slit-lamp microscopy. The contact lens is to be used in preference to the pre-set lens (Hruby). The slit lamp should be used with a very narrow beam to diagnose changes in density such as thickening of the retina, or presence of a slight elevation of the retina. With a narrow slit the subretinal fluid may appear as a translucent interval in the beam. It should also be used with a broad beam to indicate changes in color as with a localized deep hemorrhage and to search for newly-formed blood vessels behind the retina.

Careful observation of the termination of the slit-lamp beam indicates whether a slight elevation is present. If the end of the beam is concave forward the lesion is not elevated; if the beam is flat on the end or convex forward it indicates elevation.

Visual field studies may be extremely helpful in three ways. One of the principal differentiating signs between a melanoma and a nevus is the presence of a scotoma corresponding to the lesion. Usually a nevus does not disturb the choriocapillaris and thus interfere with the rod and cone function and produce a scotama, whereas a melanoma does. However, a nevus may produce a scotoma. If a scotoma is found corresponding to a lesion which appears to be a nevus, prolonged observation rather than immediate enucleation is indicated. A peripheral depression of the visual field, especially superiorly, should cause the examiner to search even more diligently for a retinal detachment. If the latter is found in the presence of a small dark lesion, the eye should be enucleated. A sector

defect in the field is associated with a hemangioma. If the retina is thickened, or its surface is uneven, and this sector defect is present, then diathermy or radiotherapy is indicated.

Of the ancillary tests used in the diagnosis of possible melanomas, transillumination is the most widely used and probably the least rewarding. The usual method of placing a bright light on the conjunctiva and gazing at the pupil from some distance away, is useless. The examiner's eye must be placed very close to the patient's eye with or without an ophthalmoscope, but with the light of the latter turned off. The light of the transilluminator must be bright and may be placed on the conjunctiva or forced between the margins of the eyelids and the orbital walls. Neoplasm, hemorrhage, and inflammation may all cast a dark shadow and are not differentiated. A neoplasm that is necrotic and cystic, or flat and light may transilluminate well. If the light is too dim, the lesion may not be seen; if it is too bright, diffusion may obscure the lesion.

Elevation of the ocular tension is sufficiently rare that it is of no help in the diagnosis. Although small tumors are very occasionally associated with an elevated tension, usually the tumor is sufficiently large that it does not come within the scope of this paper.

Aspiration biopsy has only been performed on a few patients because the procedure is frequently unsatisfactory and is potentially dangerous. It is often impossible to make a definite diagnosis from the few cells obtained. The advocates admit that a negative result means nothing. There is danger of extrabulbar extension through the puncture wound. Because of this danger immediate enucleation is recommended if the biopsy is positive, but if it is negative there is a definite possibliity of having disturbed a tumor which was not detected. It is probably that this method of diagnosis is less reliable than good clinical judgment.

Recently the uptake of radioactive phosphorous (P-32) has been used as an aid in the diagnosis of possible melanomas. The pitfalls in the P-32 test are numerous: Certain tumors, probably necrotic and cystic ones, do not take up P-32 as well as other tumors; a misleading high count may be obtained if the counting probe is placed over tissues with a relatively high vascularity and metabolism, such as rectus muscles or ciliary body. If the tip of the counting probe is not placed close to the lesion few, if any, of the radioactive beta particles from the P-32 will register. Because of these difficulties the use of P-32 in the diagnosis of intraocular tumors is certainly no more accurate than good clinical judgment, and probably not as good. It is a test that is useful as an ancillary diagnostic tool, not as the one which gives the final decision.

Comment: The author justly emphasizes the importance of obtaining complete clinical picture by means of all available ancillary methods of examination, without overemphasis of a single one before reaching a definite conclusion in the differential diagnosis of dark-appearing fundus lesions. The most rewarding method remains a skillful ophthalmoscopy supported by split-lamp study, with narrow and broad beam, of the posterior segment, and judicious interpretation of these findings.

Regarding the differential diagnosis between a pigmented lesion of inflammatory origin

and a malignant melanoma of the choroid, the opposite of the statements made in the above text is true in this commentator's experience. An increase in size with increasing blurring of the outlines of a lesion is, among others, a finding suggestive of a tumor. It is caused by an increasing retinal separation over and around the tumor, and may be associated with the very striking phenomenon of shadows cast by the retinal vessels coursing over this region. Wavy distortion of these shadows cast through a translucent subretinal fluid upon a solid background, often gives information about the knobby irregular surface of this background suggestive of a tumor.

On the other hand, the transition of an inflammatory lesion from the acute to the subacute and chromic stage will be characterized by a gradual disappearance of the collateral retinal edema and thus by an increasing distinctness of its outlines despite an occasional increase in its size.

BERTHA A. KLIEN

VITREOUS IMPLANT IN RETINAL DETACHMENT: A STUDY OF 50 CONSECUTIVE VITREOUS OPERATIONS

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Human vitreous has been planted in complicated retinal detachment cases for several years. The first successful case was operated at Manhattan Eye, Ear and Throat Hospital in June, 1949, and the retina of that patient is still attached.

The planting of human vitreous in eyes is called a vitreous implant because no vitreous is withdrawn from the patient's eye; new, sterile human vitreous is injected. This is not to be confused with vitreous transplants or replacements, such as are used for massive hemorrhages, which entail withdrawal of the bloody vitreous and its replacement by donor vitreous. The vitreous used is actually vitreous aspirate, i.e. that material which can be aspirated from a human donor eye by the suction of a syringe through an 18-gauge needle. It is a clear, transparent, oily fluid and it is not jelly-like. The donor eye is an enucleated human eye received at the Eye Bank for Sight Restoration, usually, but not always, from a deceased person. The vitreous is aspirated six to forty-eight hours after enucleation from those eyes which had corneas unsuitable for corneal transplantation. Donor eyes with neoplasm, intraocular infection, or with positive serology were not used.

The rationale of using vitreous in retinal detachment seemed logical on three different bases. A fourth factor became clinically apparent after a number of cases had been operated.

(1) *The Anatomic Basis.* The retina is attached at two points only, posteriorly at the optic nerve and anteriorly, as a ring, at the ora serrata. Between these two extremes there are only the nebulous prolongations of the pigmented cell layer. Thus, the retina extends from front to back in an arc with no proved means of support. It was felt that this support might well come from the vitreous. Therefore, any loss of vitreous volume, such as direct loss in cataract surgery, which we know predisposes to detachment, or indirectly such as subretinal fluid drainage, could lessen the retina's support. Conversely, the replenishment of vitreous volume seemed indicated to renew the support for the retina.

(2) *The Physical Basis for the Use of Vitreous.* It was felt that a logical cause of retinal detachment was the pull on the retina by the attachments of the vitreous body and consequent hole formation, as proposed by Lindner, Teng, Wadsworth, and others. If so, then the more surge of the vitreous, the more traction on the vitreous attachments. Since many retinal detachments are thought to be preceded by a detachment of the vitreous so that a highly viscous mass is surrounded by a less viscous fluid, the vitreous mass can surge freely. Therefore, the introduction of a viscous material should reduce the surge of the patient's own vitreous and consequently reduce the likelihood of subsequent detachment. Vitreous aspirate was a logical substance to form this viscous environment because it most nearly equalled the viscosity of the recipient's vitreous.

(3) *The Surgical Basis.* This is a simple hydraulic principle and can be produced by air or saline. It is effective only at the time of the injection and consists of pushing the retina back against the choroid by the mere use of pressure within the envelope of the retina. The only advantage of vitreous over air or saline is that vitreous is retained for a long time. Air is absorbed in a few days and saline is also.

(4) *Retinal Effects.* Fixed retinal folds and vitreous bands are frequently gone after a vitreous implant. Several cases with vitreous bands under obvious tension showed no evidence of the bands a week or two post-operatively. Some of these cases failed to reattach with the first vitreous implant and then, with the bands gone, reattached with a subsequent implant. The same thing happened with fixed retinal folds. The implanted vitreous has a definitely beneficial effect on the retina whether or not it reattaches from the procedure.

Vitreous implantation is best performed with the patient under general anesthesia. The conjunctiva and tenons capsule are reflected temporally, and an incision is made at right angles to the limbus through the sclera. The incision should be 4 mm. long with its center 9 mm. from the limbus. In this position entry is in the posterior portion of the pars plana away from the ciliary body and the lens. Two mattress sutures are placed edge to edge through the scleral lips of the incision. Size 5-0 monofilament nylon suture material has been found best because the knot slips easily and does not cut itself readily, as does silk and catgut.

After sclerotomy and sutures are placed, diathermy is performed. To seal the tears, nonperforating intrascleral diathermy under direct view is used to be certain the tear is isolated. The subretinal fluid is then drained. A scratch-

through incision of the sclera is made and the choroidal bleb is opened with diathermy. After drainage is complete, using suction if necessary, the donor vitreous is implanted.

Through the sclerotomy the choroid (pars plana) is opened with diathermy to avoid bleeding. The nylon sutures are made ready and held by an assistant while a syringe of 4 cc. of donor vitreous with 18-gauge needle attached is inserted. The needle is readily seen through the pupil, and vitreous is injected until the globe becomes quite firm (estimated 50 mm. Hg Schiøtz) and then is held for two minutes. The pressure is then permitted to fall to approximately 30 Schiøtz, and the nylon sutures are pulled snug and the needle withdrawn. The sutures are tied, and a ring of diathermy is placed around the sclerotomy. Any reflected muscles are reattached, and the conjunctiva is closed. The postoperative treatment is the same as for any diathermy case.

The standard of success used in assessing the results was reattachment of all of the available retina for six months or more. In 50 consecutive operations 48 per cent of 44 complicated detachments reattached, and 42 per cent of 50 vitreous implants were successful. One case had three vitreous implants, and four others had two each. Preoperative status of the 50 cases and the visual results obtained are summarized in Tables 1 through 4.

It must be emphasized that the cases presented were consecutive, and all were previous failures by other techniques. There is no selection of cases, and

TABLE 1

Preoperative Status of Cases before Vitreous Implant

Status*	Number
Saline implant plus diathermy failure	3
Scleral resecgion or other scleral surgery failures	11
3 or more previous diathermy or scleral surgery failures	14
Aphakic detachments	22
Total detachments	26
Retrolental fibroplasia	2
Fixed vitreous bands	11

* Most eyes had more than one complication.

TABLE 2

Results of Vitreous Implant Compared to Complicating Factor

Number	Complications	Per Cent Reattached
22	Aphakic detachments	31
26	Total detachments	35
18	Myopia	
	5.00 diopters or less	50
3	More than −5.00 diopters	0
11	Fixed vitreous bands	36
50	All detachments—all previous failures	42

TABLE 3

*Over-All Results of Vitreous Implant for Retinal Detachment (50 Consecutive Operations)**

Number		Per Cent
44	Complicated detachments	48 Reattached
50	Vitreous implants†	42 Successful

* Standard of success: All the available retina reattached six months or longer.
† One case had three vitreous implants; four others had two each.

TABLE 4

Visual Results of 21 Successful Vitreous Implants from 50 Complicated Detachments

Vision	No. of Cases
20/30 or better	6
20/40 to 20/70	6
20/80 to 20/200	6
Worse than 20/200	3
Total	21

many of them were truly "hopeless," particularly in the early phases of the work when the outcome or possible complications were not known.

The complications have been surprisingly few. There were no infections. There have been no major hemorrhages with this technique, although this has occurred when the vitreous implant was combined with a scleral resection. Glaucoma readily controlled by pilocarpine has developed in one case, and in this case the patient has glaucoma in the unoperated eye.

Three successful cases have slowly developed cataracts in the operated eye but only after more than two years, and in one of them there is equal cataract development in the other eye.

Several of the failures have slowly gone on to develop early phthisis but no more rapidly than is usual in old detachment cases.

Indeed, in many cases the improvement in the appearance of the retina and the reduction or absence of folds and vitreous bands are so great that the procedure appears to have a long-term therapeutic value over and above the problem of reattachment alone. Frequently the bands appear to rehydrolyze in the donor vitreous; just how this occurs is uncertain. This effect, coupled with the fact that new bands have rarely formed and never in a successful reattachment, even up to six years postoperatively, has been remarkable. Thus far, no vitreous implant eye has been lost.

Comment: The primary purpose of all retinal detachment surgery continues to be the closure of the retinal holes by means of a traumatic chorioretinitis. To achieve this, the retina must be brought in apposition to the choroid by means of an evacuation of the subretinal fluid. This is not always possible, and in recent years there has been a remarkable development of various scleral shortening procedures designed to bring the choroid adjacent to the retina.

At first glance, the implantation of human vitreous would seem to offer no great advantage over the injection of either saline or air into the vitreous cavity and mechanically forcing the retina into apposition with the choroid. It is obvious that if such procedures are to be successful, there must be adequate drainage of subretinal fluid and the author of this exciting paper has stressed this step.

The advantage of implantation of vitreous as opposed to air or saline appears to be twofold. The first is purely physical and is related to the prolonged increase in volume which is due to viscosity of the vitreous implant. The second is most intriguing and requires considerably more study before it is definitely confirmed. If implantation of vitreous can "dissolve" vitreous traction bands and fixed folds in the retina, it may possess autolytic properties which have not been demonstrated. Certainly the histologic study of vitreous bands and fixed folds of the retina would suggest permanency and the unlikelihood of any effective surgical treatment. It may well be, however, that we are unable to distinguish by means of ophthalmoscopy between permanent fixed folds and a similar picture caused by a more transient condition.

If vitreous transplant becomes a standard procedure, it is evident that far more eye bank eyes will be required than have heretofore been available.

RETROLENTAL FIBROPLASIA: COOPERATIVE STUDY OF RETROLENTAL FIBROPLASIA AND THE USE OF OXYGEN

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This study was undertaken (1) to determine whether the incidence of retrolental fibroplasia is positively associated with the duration of exposure of the premature infant to an oxygen-enriched environment, (2) to evaluate the effect on mortality of lessening the amount of oxygen given the premature infant after the age of 48 hours, and (3) to obtain information of a general nature about the premature infant and his parents that might be of use both in interpreting the data obtained and in formulating any future investigations. The plan of the study was to administer oxygen to one group of premature infants for approximately 28 days (a procedure which at the time the study was undertaken was considered routine in premature-infant care) and to restrict the administration of oxygen in a second group of infants to as little as was compatible with the clinical condition of the infant. The first group of infants will be referred to as the "routine-oxygen group," and the second group as the "curtailed-oxygen group." These two groups of infants were to be maintained in all other respects under conditions as nearly similar as possible.

There were 786 premature infants in the study. These infants represent all those born in or brought to the 18 cooperating hospital nurseries during the study year who weighed 1500 gm. or less at birth, and who survived 48 hours, at which time they were admitted to the study. Of these infants, 586 were followed for a minimum of two and one-half months: these represent the study population so far as retrolental fibroplasia is concerned.

One-third of the infants in each hospital who were admitted to the study during the first three months were assigned at random to a group that was to be given oxygen for 28 days, and two-thirds to a group that was to be given oxygen only at the discretion of the pediatrician, on the basis of clinical need. The assignments were made in matched sets of three infants. For the remaining nine months of the study all of the infants were assigned to the second group. There were 53 infants in the first, or routine-oxygen, group and 533 infants in the second, or curtailed-oxygen, group who were followed long enough to permit a diagnosis. Eye examinations were made at frequent intervals, in most instances until the infant was 6 months of age.

The mortality rates in the routine-oxygen and curtailed-oxygen groups did not differ significantly, either during the first three months of the study or throughout the entire year. The incidence of active stages of retrolental fibroplasia in the routine-oxygen group was about twice that in the curtailed-oxygen group ($P < 0.01$). The incidence of cicatricial grades of the disease in the routine-oxygen group was approximately three and a half times that in the curtailed-oxygen group ($P \ll 0.01$). The incidence of both active and cicatricial forms of retrolental fibroplasia was less for infants of single birth than for those of multiple birth. The incidence of the cicatricial form of the disease for infants of single birth was only about one-third that for infants of multiple birth ($P < 0.01$), despite the fact that infants of single birth received oxygen for two days more, on the average, and had an average gestational age two weeks less than that of the infants of multiple birth.

The incidence of cicatricial grades of retrolental fibroplasia in infants of both single and multiple birth who were in the routine-oxygen group, and whose health status can therefore be considered representative of all the infants in the study (classified as the "well" infant group), was about twice that for infants who had similarly long stays in oxygen given on the basis of clinical need (classified as the "sick" infant group). The incidence of both active and cicatricial retrolental fibroplasia increased rapidly with increased duration of exposure to oxygen for infants of both single and multiple birth. The incidence in infants of single birth increased most rapidly for exposures to oxygen of only one or two days. For infants of multiple birth the incidence increased up to periods of exposure to oxygen of about two weeks.

For all practical purposes there is no concentration of oxygen in excess of that in air that is not associated with the risk that retrolental fibroplasia may develop. Multiplicity of birth, birth weight, and, to a lesser extent, the gestational age of the infant must also be taken into account in estimating the probable risk in administering any given amount of oxygen to a particular infant, since each of these factors has been shown to influence the likelihood that an

infant will be affected by retrolental fibroplasia. Thus, infants of multiple birth appear to be significantly more susceptible to retrolental fibroplasia than infants of single birth. In addition, the figures show that generally speaking for an infant of multiple birth whose gestational age is less than 33 weeks the risk of exposure to oxygen is probably greater than it is for an infant born more nearly at term. In all infants, however, the incidence of cicatricial retrolental fibroplasia was inversely related to the birth weight.

Various miscellaneous factors, such as number of transfusions, infusions, frequency of medication, dietary adjuncts, complications of pregnancy, and the age of the mother did not appear to affect the incidence of the disease in its cicatricial form, nor did it appear that the rate of withdrawal from oxygen played a primary part in the pathogenesis of retrolental fibroplasia.

The findings obtained in this cooperative study show conclusively that the length of time the premature infant is kept in an oxygen-enriched environment is the important factor in the production of retrolental fibroplasis. Consequently, the length of time a premature infant, particularly one of multiple birth, is kept in an environment containing oxygen in concentrations in excess of that of air should be kept to an absolute minimum, consistent with the clinical indications of anoxia. When oxygen therapy is clearly required, it should be prescribed on an hourly basis and the concentration should be as low as possible.

Comment: This paper represents the concluding chapter in what is probably the most dramatic opthalmic study of this decade. Now that oxygen has been so definitely implicated in the etiology of retrolental fibroplasia, it is difficult to recall the enigma it presented five years ago.

The study by Kinsey and his collaborators seems likely to be cited for many years as a classic in medical research. Because of Kinsey's brilliant insistence upon the controlled experiment, hundreds of premature infants have been saved from blindness. Through many more years of study, it is possible that a statistical analysis of infants with and without retrolental fibroplasia would have definitely implicated oxygen as a cause. However, when the experiment began, many believed that the untreated controls, namely those not receiving oxygen or curtailed oxygen, would show an increased mortality. The study, was exquisitely designed to minimize and to correct either increased mortality or a deleterious ocular effect. The statistical design was superb so that conclusions could be made from the smallest possible sample.

Everett Kinsey, the director of this study and Arnall Patz who did the initial animal studies with newborn animals in a high oxygen atmosphere received the 1956 Lasker Award for their contribution to the elucidation of this condition.

FRANK W. NEWELL

SYSTEMIC DISEASE

OCULAR CHANGES IN PERIARTERITIS NODOSA

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Periarteritis nodosa appeared for the first time in ophthalmologic records in 1899, when P. Müller briefly mentioned the fact that in a histologic examination he "also found periarteritic changes in the blood vessels of the retina." It is interesting to note that in the ophthalmoscopic examination the eye-ground was normal. In 1926 F. Christeller reported that he had found periarteritis nodosa affecting the blood vessels of the choroid in a histologic specimen. The patient suffered from periarteritis nodosa and eventually presented an albuminuric neuroretinitis.

Since that time the clinical observations and the results of the anatomic examinations of more than 30 patients have been published. This is still a small number of cases as compared with the some hundreds observed by the general pathologist. The results of a survey show that this is partly due to the fact that the eyes are not always affected, even if the disease occurs in its generalized form. The main reason, however, seems to be that the eyes are only rarely subjected to an anatomic examination, because clinical symptoms are often lacking even though the eyeball is affected by the periarteritis nodosa. Again, it is often impossible to examine the eyes anatomically, even when clinical observation of the patient shows pathologic changes in them, and this in turn makes it impossible to establish beyond doubt the connection between periarteritis nodosa and many other noteworthy clinical observations.

The clinical ophthalmologic findings in patients with periarteritis nodosa show great diversity, but at present it seems that they can be divided into three groups: (1) changes caused by a local periarteritis nodosa of the eye; (2) changes belonging to the sequelae of periarteritis nodosa of the vascular system; and (3) active tissue changes, which according to G. B. Gruber, "may develop in addition to periarteritis nodosa, perhaps from the same cause, common to both or even quite independently of periarteritis nodosa."

The known cases, however, cannot always be classified under one of these three headings. Iridocyclitis and choroiditis, for example, have been found without the uveal vascular changes that are characteristic for periarteritis nodosa. Apparently, both iridocyclitis and choroiditis may develop without any demonstrable connection with the periarteritis nodosa; or as Gruber suggests, the inflammation may develop in addition to the periarteritis nodosa, perhaps from the same cause. If uveal inflammation occurred as a consequence of a local

periarteritis nodosa, it would belong in the first group, but if it developed without evident connection with a general periarteritis nodosa, it would belong in the third group.

The most frequent systemic finding in ocular periarteritis nodosa is an albuminuric retinitis. A survey of the literature made in 1944 showed that of 90 patients with periarteritis nodosa in whom the eyegrounds were observed 21 had an albuminuric retinitis or a hemorrhagic neuroretinitis with retinitic patches. All of these patients had albuminuria and high blood pressure. The duration of the disease had been at least three months, sometimes even more than a year, and in a few instances several years. Moreover, most of the patients were men which agrees with the observation made by Gruber that periarteritis nodosa is three or four times as frequent in men as in women.

Periarteritis nodosa of the choroidal vessels has been reported in two patients with the generalized form of the disease and albuminuric retinitis, but unfortunately no detailed descriptions of the findings were given. In a number of patients with the generalized disease, retinal detachment occurred; but since in none of these cases was it possible to perform a histologic examination at the time of the detachment, it is impossible to say whether or not the detachment was an exudative one resulting from a local periarteritis nodosa of the choroidal vessels. Such a detachment has been described for exudative choroiditis without periarteritis nodosa, or Harada's disease. Other authors have described the retinal detachment in their cases of periarteritis nodosa as an exudative detachment caused by an extensive periarteritis of the choroidal vessels: retinal detachment of this kind should be classified in the first group, that is, among the changes due to local periarteritis nodosa. In some cases, however, retinal detachment is apparently due to albuminuric retinitis.

On the basis of anatomic examinations, Friedenwald and Rones, and Boeck were able to show conclusively that the albuminuric retinitis in periarteritis nodosa does not constitute a manifestation of ocular periarteritis nodosa, but is rather a sign of the serious effects of the general disease on the kidney and the circulation.

Occasional very rare ocular changes in patients with periarteritis nodosa, such as involvement of the central retinal artery, optic atrophy, and pupillary disturbances and paralyses of the external ocular muscles, further prove the great diversity of the ophthalmologic manifestations of periarteritis nodosa, the actual cause of which is still unknown, although the interesting suggestion has recently been made that it may be caused by a virus, perhaps even by a virus closely related to that responsible for herpes zoster.

OPHTHALMOPLEGIA, STEATORRHEA, PHLEBECTASIA AND VASCULAR LIPOMAS

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An unusual combination of signs and symptoms was encountered in a 51-year-old man first admitted to the Medical Service of the University Hospitals in 1951. The patient, a clerical worker; stated that during the previous 20 years he had experienced many fluctuations in a chronic illness characterized by abdominal distention with gas, loose, foul, "putty-like" stools, and weakness. He had had many programs of therapy outlined by various physicians and clinics, consisting in the main of special attention to diet, with various combinations of liver extract, B-complex vitamins, particularly thiamine, and later vitamin B_{12} and a regimen of rest. Remissions and exacerbations had occurred, but in his opinion they were entirely unrelated to therapy. A year before admission he began to note a drooping of his left eyelid and at the same time he had increasing difficulty in focusing his eyes. Diplopia on lateral gaze then occurred. His hands and feet often felt cold and numb. At the time of admission he was having not more than two or three loose stools a day and his appetite was good. His main complaint was an overwhelming and progressive weakness which was now worse than ever. He was so unsteady on his feet that he was unable to walk. The right pupil was slightly smaller than the left, but both reacted to light. Convergence was impossible and there was extreme drooping of both lids so that he had to tilt his head back to look straight ahead. Very prominent veins coursed over the abdomen, chest, back, and extremities. Scattered at various points beneath this network of veins were lesions that felt like lipomas or fibromas.

On the basis of these and other physical findings, as well as the results obtained by laboratory and x-ray tests, members of the medical and neurologic staffs agreed that this patient had Wernicke's syndrome, as well as posterior column degeneration of the cord. Myasthenia gravis was excluded by appropriate tests. Treatment with thiamine and other B-complex vitamins was tried without success, although the hemoglobin level, which had been 8 gm. per 100 ml., was raised to 11 gm. per 100 ml. after the administration of iron by mouth and four 250-cc. blood transfusions. Various diets were tried, but the patient did better when he chose his own food, using his judgment based on long experience in varying his diet. For short periods his diarrhea and abdominal discomfort would decrease, and then recur for no apparent reason.

Biopsy of the partially compressible tumors connected with the veins revealed them to be vascular lipomas. These mesodermal tumors had their vascular components well demarcated. Although the vascular element predominated, the presence of much adipose tissue led to its classification among the vascular

lipomas. The major element was certainly angiomatous with only a relatively small amount of lipomatous tissue. The pattern of veins over the abdomen was that of a general reticular network of large veins. It was not the kind of pattern found with obstruction of either vena cava. In some instances it is difficult to decide whether prominent veins over the abdomen merely appear larger than normal because of loss of subcutaneous tissue or whether there is a real increase in size and pressure. The veins in this patient stood out prominently everywhere. Some of this was the result of great wasting of subcutaneous tissue, but they were much more prominent than those seen in patients with anorexia nervosa or the terminal stages of cachexia of cancer.

Although the findings strongly suggest Wernicke's syndrome with lesions in the nuclei of the oculomotor nerves, it may be that the peculiar combination of lesions found in this patient represent a new syndrome.

ZOONOSES IN OPHTHALMOLOGY

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The list of zoonoses found in Australia which are accompanied by ocular complications includes scrub typhus and Q fever (bandicoots), cat scratch fever (cats), bovine tuberculosis and brucellosis (cows), hydatids (dogs), Newcastle disease (fowls), Molluscum contagiosum (parrots), trichinosis (pigs), toxoplasmosis (rabbits), and Leptospirosis Australis A & B (rats). An additional reservoir of scrub typhus is found in rats. This list, though incomplete, gives a general outline of the scheme of animal disease in this large continent.

So far, the only success achieved in the war on zoonoses seems to be the reduction of bovine tuberculosis. Efforts to destroy the pests harbored by domestic animals and pets, however, must go on, and ophthalmologists should take an active part in them.

The infantile form of toxoplasmosis with its distinctive characteristics of microphthalmos, typical choroidoretinitis, cerebral calcification, and hydrocephalus with epileptiform fits, can hardly be mistaken now. The active adult form is much more difficult to detect, especially as the dye test cannot be made in Australia and the skin test is hardly sensitive enough to warrant a diagnosis. Nevertheless, four cases of the adult form were reported in 1952. Undoubtedly in the past many cases of toxoplasmosis were erroneously diagnosed either as syphilis or as tuberculosis. The spread of the disease is a puzzle. The organism is harbored by many animals and birds and apparently adult human beings may contract the disease with a variety of extensive reactions. Even in the most active

cases in adults, however, there is no clue as to the site of entry except in experimental laboratory workers who have punctured their fingers with an infected needle.

Newcastle disease has so far been reported as producing only a conjunctival lesion, and most of the cases have occurred in laboratory workers. The author, however, feels that it can produce a relapsing uveitis and he believes that it may have a close relationship to disseminated sclerosis. This is a possibility that needs careful investigation and controls.

Cat-scratch fever in its general aspects has been dealt with extensively in the literature, and evidence has been produced to show that the same causative agent is probably responsible for Parinaud's oculoglandular syndrome. Intensive penicillin therapy brought about a rapid recovery from an acute case of this syndrome in a patient with a history of cat scratch lately observed by the author.

Molluscum contagiosum is a skin disease of children or adults which is not easily mistaken when seen. The upper eyelids and face are particularly affected, but fortunately curettage and cauterization provide a simple and not disfiguring cure.

Q fever, caused by Rickettsia burneti, and the allied tick-borne fever caused by R. australis are characterized by specific agglutination reactions and can therefore be identified in suitably equipped laboratories. The ocular complications of Q fever consist chiefly of pain in various forms—retro-orbital pain, pain on movement or pressure, photophobia, and conjunctival irritation—although diplopia and signs of encephalitis have also been seen and an occasional patient may show episcleritis or some other rare complication. Q fever responds dramatically to antibiotics, especially terramycin. By contrast, the ocular complications of australis infection are purely conjunctival.

Iridocyclitis due to leptospirosis australis has so far not been reported in the Australian literature, but the periodic ophthalmia in horses found in the river valleys in New South Wales is believed to be leptospiral in origin, and many cases of leptospirosis have been reported from Wewak in New Guinea. The diagnosis of leptospirosis is fairly straightforward and conclusive if the following techniques are available in the laboratory: dark-field examination, cultural tests, animal inoculation, and the serologic test.

Brucellosis, which appears chiefly in the form of Brucella abortus in Australia, is far more widely recognized by the veterinarian than by the clinician. If the routine laid down by Dean Foggett (1954) were followed in all doubtful cases of corneal and uveal inflammation, the picture of brucellosis and ocular disease might be much clearer. In New Zealand, which is a great dairy country, the ocular diagnosis is difficult, as the eye complication often appears six months after the beginning of the general disease and by this time the agglutination test results are doubtful.

Bovine tuberculosis is virtually nonexistent in human beings in Australia, and the rate of its incidence in New Zealand has remained stationary at 0.4 per 10,000 population for the last eight years. Ophthalmic surgeons of the present day probably never see a case of conjunctival tuberculosis.

Hydatid disease of the brain with ocular signs seems to be much more common in Australia than hydatid disease of the orbit. Dew (1955) reported 10 cases of cerebral hydatid, in 8 of which papilledema was present and in 5 homonygmous field defects, so that the diagnosis and localization of hydatid disease of the brain is very much an ophthalmologic project. Hydatid disease is a public health problem, and it should be just as possible to stamp out this condition as it was to eradicate yellow fever from the Canal Zone.

About 40 per cent of the persons in whom trichinosis produces pathologic lesions present eye symptoms. First of all, there is lid and orbital edema with myositis of the eye muscles together with the larvae of Trichinella spiralis appearing subconjunctivally and retinally. The larvae are often found in the retinal hemorrhages. High temperatures with high eosinophilia and acute orbital edema should lead to immediate consideration of trichinosis as a diagnosis. No treatment helps this disease, and retinal hemorrhages have a bad prognosis. Prevention is therefore essential and all pork food must be thoroughly cooked to destroy the parasites.

Scrub typhus, also known as Japanese river fever or flood fever, is caused by Rickettsia Orientalis and is transmitted by mite vectors. The chief reservoirs of the mites in New Guinea are rats and bandicoots. The disease, which has all the symptoms of an acute infection, usually ends with lysis on the 14th day. The only ocular complications reported, other than subconjunctival hemorrhages, which have a bad prognosis, are bilateral optic neuritis (1 case in 130) and retinal vein thrombosis (3 cases in a review of 326 cases). Chloramphenicol, chlortetracycline, and oxytetracycline were all found by Ley and Smadel (1954) to be equally efficacious in the treatment of this deadly disease. From their report it seems probable that the early application of broad spectrum antibiotics will eliminate all ocular complications.

The whole problem of uveitis and its diagnosis in relation to zoonoses should be restudied in the light of modern advances.

HEREDITARY DISEASE

CONGENITAL SEX-LINKED PSEUDOGLIOMA AND GRAVE MENTAL DEFICIENCY

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Acta ophth., 1956, *34:* 250–254

Pseudoglioma is the term used to designate all the conditions which, though not true glioma, produce the symptom of "amaurotic cat's-eye" in children. Among the causes of this disorder are various inflammatory conditions, such as metastatic ophthalmitis, tuberculosis, syphilis, and parasitosis. Another large group of causative conditions may be found in developmental anomalies. These may appear as the result of stagnation in embryonal development with persistent vascular capsule of the lens, hyaloid system, or primary vitreous body. Consequent complications in these cases are connective tissue proliferations, microphthalmos, cataract, and varying degrees of amotio retinae, all of which make this group quite a heterogeneous one. Certain facts, however, indicate that a retinal defect may often be the primary cause. Thus isolated amotio occurs as a hereditary defect leading to something that closely resembles pseudoglioma. Benign tumors, angiomatoses, organized hemorrhages, retrolental fibroplasia in the premature, and Coats' retinitis may be mentioned as other causes.

Cases of pseudoglioma with probable sex-linked transmission have been published by various authors and the interesting hypothesis has been suggested that falciform detachment, juvenile cystic detachment, vascular opacities in the vitreous body, and certain types of pseudoglioma form a clinical unit with sex-linked heredity. According to Sorsby (1951) these anomalies might be considered as different stages of the same disease.

Malformations typical of pseudoglioma, associated with grave mental deficiency, were found in three patients, an uncle and two nephews. Their family pedigree, which shows an additional case of blindness in a maternal uncle of the first patient, supports the belief that pseudoglioma is a developmental malformation inherited recessively and by sex-linked transmission. Findings common to the eyes of all three patients were small bulbs, shallow anterior chamber, atrophy of the iris, synechias, a vitreous body filled with a grayish white vascularized tissue, and secondary cataract. The tumorous formations in the fundus were apparently primary; the other malformations had a secondary origin. No pathologic-anatomic investigations have been made and it is therefore difficult to make accurate statements about the character of the malformations. The picture of bilateral pseudoglioma was present at birth and stagnation of embryonal development may be considered an explanation of the malformations.

Comment: Dr. Dahlberg-Parrow's paper is a valuable contribution to the literature dealing with the inherited anomalies of retinal development. Congenital falciform detachment, congenital pseudoglioma, and congenital cystic detachment are entities known to be hereditary. The most common mode of transmission is sex-linked recessive (Roberts 1937; Wilson, 1949; Sorsby, 1951). Sjogren, however, suggests the probability of partial sex-linkage while Weve believes that a simple autosomal transmission cannot be excluded.

Mental deficiency is a component seen in many of the syndromes having associated ocular involvement. In fact, nearly 50 per cent of the reported cases of microphthalmos and anophthalmos have had associated mental deficiency. An unreported family of ours exhibiting sex-linked recessive congenital total retinal detachment, on the other hand, has associated deafness. Thus, it appears probable that many of the above-mentioned retinal developmental aberrations may be variants of a similar gene. In particular families or in different genetic milieux this gene may effect or be associated with mental deficiency and deafness.

The simple but routine expediency of the ophthalmologist inquiring about other members of the patient's family being similarly affected will not infrequently save that individual much needless expensive diagnostic procedures as well as perhaps a disfiguring enucleation.

HAROLD F. FALLS

THERAPEUTICS

STERILITY OF EYEDROPS

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Ophthalmologica, 1956, *132:* 167–171

An investigation into the cause of an epidemic of Bacillus pyocyaneus ulcers in the Rotterdam Eye Hospital revealed the fact that many of the eyedrops used at the Clinic at that time were contaminated with the Gram-negative B. pyocyaneus, in ophthalmology the agent of a highly refractory corneal ulcer. Both penicillin and albucid were infected, but this is not surprising since these drugs are known to have no influence on Gram-negative bacteria. The stock was not infected. The logical conclusion was that contamination occurred during use. In the investigation all the ointments used were found to be free from bacterial infection.

These findings led to an inquiry into the sterility of eyedrops in routine use and possible measures for keeping them sterile. The first requirement, of course, is that the eyedrops should be sterile during preparation. It must be remembered that a preservative agent for eyedrops should, if possible, possess the following properties: (1) It should not cause lesions or irritation of the cornea and conjunctiva, or give rise to hypersensitivity. (2) Its activity should be maintained during sterilization of the eyedrops and in the presence of the active agent of the eyedrops, and it should not impair the effectiveness of the eyedrops themselves. (3) It should be a fungicide as well as a bactericide. (4) It must act quickly (30 to 60 minutes). After a review of the literature on the subject, zephiro (1:25,000) and phenylmercury nitrate (1:25,000) were selected for addition to the eyedrops in all departments of the Rotterdam Eye Hospital. Phenylmercury nitrate is still used in eyedrops, but zephirol only is now used in normal saline solution, as phenylmercury nitrate attacks the aluminum caps of the bottles and produces a sediment.

Weekly culturing of eyedrops, as well as hourly sampling, have not revealed any contamination since the disinfectants have been in use. It is conceivable that the risk of infection of eyedrops by contact with eyelashes, fingers, eyelids, and skin is greater in a large outpatient department which is at the same time a training center for medical students, many of whom have had little or no experience in the technique of applying eyedrops. Infection may also exist in the private consulting rooms of ophthalmologists, as shown by the fact that in 9 of 12 such centers in which a similar investigation was made one or more preparations were found to be contaminated with Gram-negative or Gram-positive bacilli, Gram-positive cocci, or fungi. Two of the three ophthalmologists who had sterile eye-

drops used a disinfectant as a routine measure and the third renewed his stock every week.

Comment: Dr. Goettsch's article touches on a very important phase in the administration of ophthalmic drugs. Considerable research work has been expended in solving this problem. It is obvious that the perfect protective agent has not yet been found. Eye solutions must be protected against the growth of molds, bacteria, and viruses. Not only must they be sterile when dispensed, but the solution must be protected from contamination during its period of usefulness. There is also the problem of using a preservative which inhibits the growth of bacteria but does not prevent their rapid multiplication when instilled into the eye. The best preservatives are those which are bacteriocidal.

Mold growth can usually be prevented by storage in a refrigerator. Cold solutions are uncomfortable for immediate use.

Among the preservatives which have been used in ophthalmic solutions are chlorbutanol (0.35 per cent to 0.5 per cent), esters of parahydroxybenzoic acid such as propylparaben and methylparaben (0.1 per cent), benzalkonium chloride (zephiran chloride 1:10,000 to 1:50,000) (of doubtful value against pseudomonas aeruginosa), sodium formaldehyde sulfoxylate (1:5000), sodium sulfite (0.1 per cent) in the anhydrous form. These latter two are suggested as antioxidants. Mercuric oxycyanide 1:1500, recommended for use with dionine; phenyl mercuric nitrate 1:2500 to 1:10,000. This latter agent has been suggested for use with eserine and epinephrine. Phenyl alcohol in 0.5 per cent strength may also be used. It seems a wise precaution for the ophthalmologist who is anxious to avoid spreading infection to use disposable droppers so that no dropper is ever reinserted into the parent solution after it has been used to instill the agent into the patient's eye. Another helpful method is to change each solution frequently.

Each of the recommended preservatives has disadvantages. Goettsch mentioned that the merchlorocresol 0.1 per cent strength gives rise to irritation. Chlorbutanol was found by Klein to lose its activity when heated, and phenylmercuric nitrate attacks the aluminum caps of bottles. Zephiran, besides not being compatible with nitrates and salicylates is of doubtful value against ps. aeruginoses. Many of the quarternary ammonium compounds produce hypersensitization and are somewhat damaging to the cornea in bacteriocidal concentrations.

Regardless of the preservative employed and methods for initial sterilization of the solution, it is necessary that the ophthalmologist be aware of his responsibility to avoid spreading any infection. He cannot rely solely on preservatives. This is especially true in diseases such as epidemic keratoconjunctivitis where fingers, instruments, such as tonometer, as well as contaminated solutions and droppers have aided in the transmission of the disease.

IRVING H. LEOPOLD

UVEITIS

UVEITIS AND RHEUMATIC DISEASES

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Ann. Rheum. Dis., 1956, *15:* 140–150

Few attempts have been made to assess the extent of the association between uveitis and rheumatic diseases. Among the rheumatic diseases found in patients in whom their presence was investigated were spondylitis, with a reported incidence varying from 2.4 to 25.6 per cent, and rheumatoid arthritis, found by Vesterdal (Acta ophth. 1951, *29:* 509) in 20 per cent of her patients, but not reported by any of the other authors. In none of these studies was a diagnosis of Reiter's disease made, but clinical or serologic evidence of "gonorrhea" was found, again by Vesterdal in 23 (19.2 per cent) of her patients, and 16 of them (69.4 per cent) had arthritis.

The reported incidence of uveitis in patients with rheumatic disease has varied widely. Estimates of its occurrence in association with ankylosing spondylitis range from less than 10 per cent in one series to slightly more than 40 per cent in another when patients over 45 years of age who had had their disease for 15 years or more were considered. Conjunctivitis is the commonest reported ocular manifestation of Reiter's disease, but iritis may occur and relapsing iritis has been reported in 6 patients with recurrent or chronic arthritis associated with veneral urethritis. The highest reported incidence of uveitis in rheumatoid arthritis is only 4.7 per cent, and in acute rheumatism it is generally admitted to be rare.

As part of a wider survey of the etiologic factors concerned in uveitis conducted by one of the authors, a study was made of all the patients attending the outpatient clinic of the University Department of Ophthalmology between January, 1953, and June, 1955, suffering from uveitis, excluding those with frankly purulent infections (panophthalmitis), postoperative uveitis, and kerato-uveitis in which the uveitis was relatively mild and apparently dependent on the accompanying keratitis (e.g., uveitis associated with septic corneal ulcers). Those with kerato-uveitis in which the uveitis formed a major part of the disease picture, and appeared to progress independently of the keratitis, were included in the series. No patients had been referred directly from the Rheumatism Centre to the Eye Department.

The patients were routinely referred to the Rheumatism Centre, where a complete clinical examination was made of the limbs and spine. Almost all the patients were examined by one of two observers who were unaware of the exact

type of uveitis present. Radiographs were made only when considered indicated on clinical grounds. The sheep cell differential agglutination test for rheumatoid arthritis (D.A.T.) was carried out and agglutination at a dilution of 1:32 or more at 18 hours was taken as a positive result.

The ocular disease diagnosed at the patient's first attendance was classified as kerato-uveitis, anterior uveitis (iritis or cyclitis, alone or together), posterior uveitis (choroiditis with or without cyclitis), or pan-uveitis (iritis, cyclitis, and choroiditis). The anterior uveitis group was further subdivided into three types: (1) granulomatous, characterized by an insidious onset and chronic course, organic changes in the iris, a tendency to form posterior synechiae, and keratic precipitates on the back of the cornea; (2) nongranulomatous, with an acute onset and relatively short duration, edema of the iris without gross organic changes, copious but easily absorbed exudate into the anterior chamber, posterior synechiae that are not marked except after recurrent attacks, and small keratic precipitates; and (3) doubtful. The prognosis in individual attacks of nongranulomatous anterior uveitis is relatively good, but the condition tends to recur and may then lead to permanent loss of vision.

The patients were also classified into those with and those without a known nonrheumatic cause for the uveitis. Uveitis was taken to be of nonrheumatic origin when it was associated with herpes zoster ophthalmicus, dendritic ulceration of the cornea, interstitial keratitis, secondary syphilis, superficial punctate keratitis, sarcoidosis, sympathetic ophthalmia, rupture of the lens, heterochromic cyclitis, and Vogt-Koyanagi syndrome.

The main classifications of rheumatic disease employed were osteoarthritis, rheumatoid arthritis, Reiter's disease, and "spinal arthritis." The category of osteoarthritis, was further subdivided into degenerative joint disease and "generalized" osteoarthritis as described by Kellgren and Moore (Brit. M. J. 1952, *1:* 181) "spinal arthritis" was subdivided into ankylosing spondylitis and "atypical" spondylitis. The remaining rheumatic diseases, using the term in a broad sense, were grouped together as "other diseases." In a few patients it was not possible to make a differential diagnosis between Reiter's disease, rheumatoid arthritis, and ankylosing spondylitis. In some cases, osteoarthritis coexisted with one of these conditions. If rheumatoid arthritis entered into the differential diagnosis, it was considered the main rheumatic disease; similarly, Reiter's disease was given preference over ankylosing spondylitis, and each of these three conditions was listed as the main diagnosis in preference to osteoarthritis.

The data obtained did not show any particular association between uveitis and psoriasis, acute rheumatic fever, generalized osteoarthritis, or degenerative disease of the limbs and spine. The failure to find any significant association of rheumatoid arthritis with uveitis is of greater interest. Although undoubtedly patients may occasionally be encountered in whom the uveitis is associated with changes in the cornea and sclera similar to those in the connective tissues elsewhere in rheumatoid arthritis, the association in most cases is probably coincidental.

The findings confirm the association of unilateral nongranulomatous anterior

uveitis with ankylosing spondylitis, of which it may be the initial symptom. In only three of the patients suffering from ankylosing spondylitis with radiographic confirmation was the uveitis of the doubtful type, and granulomatous uveitis was not seen in any of them. Ankylosing spondylitis occurred in 30.8 per cent of the males and in 22.6 per cent of all the patients with nongranulomatous anterior uveitis examined for rheumatic disease; the total incidence of ankylosing spondylitis, including those patients with atypical spondylitis in whom ankylosing spondylitis could not be definitely excluded, may have been as high as 49.0 per cent in males and 35.6 per cent in all patients with this type of uveitis. The incidence in uveitis of the doubtful type was about half that in the nongranulomatous type. The failure of some earlier observers to find a marked association of uveitis and ankylosing spondyltis may have been due to the relative mildness of the rheumatic symptoms in many cases, so that full clinical and radiologic examination is required for diagnosis.

Nongranulomatous anterior uveitis was found to be associated with rheumatic diseases in which involvement of the spine is a feature, namely, spinal arthritis and Reiter's disease. This raises the possibility of a connection between this type of uveitis and a factor common to these rheumatic diseases which is perhaps related to the spinal involvement. In uveitis as a whole, these diseases occurred in about one patient in four.

Comment: The association of uveitis of the nongranulomatous variety with ankylosing spondylitis has been well documented in the literature. The present findings confirm this observation. The incidence (23–35 per cent) of ankylosing spondylitis in this series of patients with nongranulomatous uveitis is suprisingly high, however.

As pointed out by Vesterdal and confirmed by the present authors, x-rays of the spine are necessary to establish or reveal the diagnosis of ankylosing spondylitis. It is apparent that such radiologic examinations should become part of the routine workup of all patients with nongranulomatous uveitis.

A number of reports have appeared in the literature of the association of rheumatoid arthritis of the extremities with nongranulomatous uveitis. In fact this has become a part of ophthalmologic teaching. The present authors found evidence of rheumatoid arthritis in 11 per cent of the 221 patients with uveitis, but feel that this incidence was no higher than that in a comparable group of their patients without uveitis. They conclude, therefore, that the alleged association of rheumatoid arthritis and uveitis is coincidental.

However Thompson and Eadie found uveitis in 3.3 per cent of a series of 210 patients with rheumatoid arthritis and Bauer reported an incidence of uveitis in 4.7 per cent of rheumatoid arthritis patients. In a series of 120 patients with acute fibrinous iridocyclitis Vesterdal noted rheumatoid arthritis in 20 per cent. These findings would appear to be beyond the realm of coincidence.

In the past emphasis has been placed upon the conjunctivitis associated with the urethritis and arthritis of Reiters Syndrome. In the present uveitis series, 16 patients (7 per cent) had Reiters Disease.

In this report of Stanworth and Sharp, it is of considerable interest that of 83 patients studied with *anterior* nongranulomatous uveitis, more than half had some type of rheumatoid involvement (rheumatoid arthritis 11 per cent, Reiters Disease 7 per cent, and spinal arthritis 35 per cent). These findings are of even greater interest when considered in

conjunction with the evidence presented by Alan Woods of a high incidence of streptococcal hypersensitivity in this group of uveitis patients. Studies in patients with rheumatoid arthritis have revealed similar relationships to streptococcal infections. The recent reports of elevated antistreptolysin and antihyaluronidase titers, and the appearance of C-reactive proteins in the blood of patients with uveitis, also tend to confirm the role of the streptococcus in the pathogenesis of nongranulomatous uveitis and rheumatoid arthritis.

BERNARD BECKER

A COMPARISON OF THE TOXOPLASMIN SKIN TESTS, THE SABIN-FELDMAN DYE TESTS, AND THE COMPLEMENT FIXATION TESTS FOR TOXOPLASMOSIS IN VARIOUS FORMS OF UVEITIS

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Bull. Johns Hopkins Hosp., 1956, *99:* 1–15

Acquired toxoplasmosis is now generally conceded to be an important cause of granulomatous uveal disease in adults; in addition, the results of skin and dye tests in patients with toxoplasmosis are known to be usually positive. In the individual clinical case, however, it is extremely difficult to evaluate the significance of the positive cutaneous and serologic tests, and there is no generally accepted criterion for a firm clinical diagnosis of acquired adult ocular toxoplasmosis. The difficulties arise from the relatively high incidence of positive results in apparently normal healthy individuals, the possible non-specificity of the dye test, the improbability of isolating the parasite from the blood or extraocular tissues, and the absence of any associated systemic symptoms of infection with the parasite.

In the hope of resolving some of these difficulties, an analysis of the results of the toxoplasmin skin tests and of the serologic tests for toxoplasmosis has been made in 193 uveitis patients studied in the Wilmer Institute between July 15, 1953, and July 1, 1955. In all these patients a diagnosis of either nongranulomatous or granulomatous uveitis was made on the first ophthalmologic examination. A diagnosis of nongranulomatous uveitis believed due to an allergic insult was made in 86 of the patients, and the remaining 107 were given a diagnosis of granulomatous uveitis believed due to an infection of the uveal tract with some pathogenic agent causing granulomatous disease. Many of the patients with

nongranulomatous uveitis were in periods of remission between attacks, and the eyes were quiet. Practically all the patients with granulomatous uveitis were in the active stages of the ocular disease. There was no particular difference in the age distribution of the patients in the two groups.

The diagnostic criteria employed for the diagnosis of ocular toxoplasmosis in the individual case were (a) an ocular picture believed compatible with Toxoplasma infection; (b) the exclusion of other systemic granulomatous infections to which the condition might be ascribed; and (c) the presence of a positive toxoplasmin skin test together with a dye test positive in a minimum titer of 1:64. Under these criteria, 37 cases or 35 per cent of the 107 cases of granulomatous choroiditis were attributed to toxoplasmosis.

When the results of the tests were analyzed, it became clear that the complement fixation test was of little or no value except during the course of an acute infection. Although the incidence of a positive diagnosis of ocular toxoplasmosis is not greatly affected by lowering the standards for a significant dye test to positive in titers of 1:32 or even of 1:16, the evidence available from this study indicates that a dye test titer of at least 1:64 may reasonably be expected in an individual with active ocular toxoplasmosis, and it is unwise at present to reduce the criteria for a significant test below this level. In the overall picture, with the dye test considered positive only at titers of 1:64 or higher, there was 80 per cent correlation between the skin and the dye tests, that is, either both tests were positive or both were negative.

There was no correlation, on the 1:64 dye test titer basis, between the skin and the dye tests in 16 patients with granulomatous uveitis. If titers of 1:16 were considered positive, there were only two patients with granulomatous uveitis who had positive skin tests and negative dye tests. In the entire series, there was a 72 per cent incidence of positive dye tests among the patients who had positive skin tests. When the standards for a positive dye test were lowered to 1:32 and to 1:16, this incidence rose to 76 per cent and 90 per cent respectively. When granulomatous cases only were considered this incidence of positive dye tests under the three standards (1:64, 1:32, and 1:16) in patients with positive skin reactions was respectively 85 per cent, 90 per cent, and 95 per cent. High intensity skin tests and high titer dye tests appeared to be more frequent in the acute forms of ocular toxoplasmosis, although the evidence on these points is inconclusive.

Ocular lesions attributable to toxoplasmosis were found in 37 patients in the present series and in 42 patients in another series previously reported, making a total of 79 cases of adult ocular toxoplasmosis. The types of ocular disease represented were focal choroiditis or chorioretinitis, 51; old granulomatous chorioretinitis with a secondary acute allergic reaction superimposed upon it, 7; generalized uveitis, 17; and retinal periphlebitis, 4.

Information was available on the effect of treatment with Daraprim and sulfadiazine in 22 cases: in 13, the response was favorable; in 3, the improvement was questionable, and in 6 the treatment was ineffectual. Severe side-reactions occurred in four patients, one of whom required several transfusions before

recovering from agranulocytosis. Side-reactions also occurred in four other patients, but were relatively insignificant in character.

Comment: This paper has practical significance for the great majority of ophthalmologists who do not have nearby facilities for serologic tests in suspected ocular toxoplasmosis. The author's figures indicate that if a patient with granulomatous uveitis has a positive toxoplasmin skin test, that patient has a 95 per cent chance of having a positive dye test in a titer of 1:16; a 90 per cent chance, in a titer 1:32; and an 85 per cent chance, in a titer of 1:64. Even if the last figure is used as the criterion for a diagnosis of ocular toxoplasmosis, a positive skin test constitutes strong presumptive evidence in favor of this diagnosis. A negative skin test does not have the same value in excluding toxoplasmosis, since of granulomatous uveitis patients whose dye test was positive in a 1:64 titer, 15 per cent showed a negative skin test.

HENRY F. ALLEN

Basic Sciences

BACTERIOLOGY

OPEN PROBLEMS AND RECENT DEVELOPMENT IN OCULAR VIROLOGY

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Boll. d'Oculistica, 1956, *35:* 161–180

The rate of virus infections has been increasing with respect to that of infectious diseases in general, mainly because there has been a decline in the rate of bacterial diseases as the result of chemical and antibiotic therapy. Trachoma is the most important virus disease from the ophthalmologist's standpoint. It is caused by a peculiar, large virus that is filtrable and can be seen, though with some difficulty, with the common microscope; its developmental cycle is completed in 24 to 48 hours. Attempts at cultivating this virus with several techniques have given incomplete and indefinite results. The author was unable to transmit trachoma after the virus had been cultured in the vitelline sac, despite the fact that the erythrocyte agglutination test according to Hirst was in some ways positive in the embryonal fluids of infected eggs.

The localization of the trachomatous virus constitutes a great problem. Inclusion bodies and other elements characteristic of trachoma have been found in the epithelium only, yet the anatomicopathologic lesions of the disease reach the conjunctiva and the tarsus. This finding can only be explained by the existence of either nonviable forms of the virus or of a toxin that is manufactured in the epithelium and that transpasses the epithelial barrier. If, as seems likely, only the epithelial tissue is capable of transmitting trachoma or of harboring its virus, the second of the two hypotheses appears more probable. As to the relationships between trachoma and inclusion conjunctivitis, Bietti, unlike Ishihara and coworkers, does not believe the two viruses to be identical and the different clinical aspects in the adult (trachoma) and the child (inclusion ophthalmoblennorrhea) to be the result of a different conjunctival reaction owing to age. In agreement with Lindner, he considers trachoma and inclusion conjunctivitis to be, like the virus of measles and smallpox, closely related but not identical. Correlations have also been found between the causative agents of trachoma and inclusion conjunctivitis on the one hand, and those of the group venereal lymphogranuloma-psittacosis on the other. There seem to exist between the two groups phenomena of crossed immunization, but there are also differences.

With regard to the therapeutic problem, the current most practical and most effective treatment of trachoma is the oral administration of small or average

doses of sulfonamides (40 to 60 mg. per kg. of body weight) in three monthly cycles of three weeks each and the application of active antibiotics on the virus and the bacterial flora in the conjunctival sac several times each day during the entire treatment period. Recent investigations of the author proved that cures thus obtained are generally definitive, even after years, although reinfections may occur. The introduction of N-N′ di-benzylethylendiamine dipenicillin G has simplified the problem of quick mass treatment of the condition. He obtained complete disappearance of the conjunctival granuloses in 67 per cent of patients and almost complete disappearance in 18 per cent with the daily intramuscular injection of 2,000 to 2,500 units per kg. of body weight in 5 to 7 injections every two to three weeks (a total of 5,000,000 to 6,000,000 units to a 20 kg. child). Sulfonamides incorporated in oil are also being tried at his clinic.

As to the ocular manifestations of conditions caused by Chlamydozoa, while those of psittacosis and other virus pneumonias are extremely rare, venereal lymphogranuloma may cause Parinaud's conjunctivitis with characteristic secondary adenopathy, palpebral and episcleral cutaneous lesions owing to photosensitization, secondary keratitis and uveitis. A form of Parinaud's conjunctivitis with secondary lymphadenitis has been ascribed to the virus that causes benign lymphoreticulosis.

The next most interesting virus disease from the ophthalmologist's point of view is herpes simplex. The most important ocular localization of this virus is in the cornea with superficial forms—the classical vesicular keratitis of Horner, dendritic keratitis, superficial herpetic punctate and striate keratites, herpetic filamentous keratitis, relapsing ulcerations of the cornea and marginal and paramarginal herpetic ulcers, bullous keratitis and herpetic neuroparalytic keratitis—and deep forms—herpetic disciform keratites and deep diffuse keratites in addition to some sclerosing keratites and the so-called posterior herpes of the cornea with small vesicles protruding into the anterior chamber. The so-called "metaherpetic keratitis" should also be included among the deep forms. Herpetic manifestations of the uvea are less known than those of the cornea. There are also inflammatory localizations of the herpetic virus to the optic nerve and lesions to the ocular nervous system. Except for cauterization, the treatment of herpetic lesions to the cornea is poor. This is ascribed to the characteristics of the virus, i.e., to its lack of an autonomous metabolism. The virus of herpes zoster is also of interest to the ophthalmologist for its frequent localization in the area of distribution of the first branch of the trigeminus nerve with concurrent conjunctival, scleral and episcleral, corneal, uveal, retinal lesions, lesions to the optic nerve and optic pathways and even hemiplegia as well as glaucoma. Ocular manifestations may also be seen in chickenpox, smallpox, influenza and sometimes in infectious mononucleosis and epidemic hepatitis. Of some importance are also ocular manifestations of measles, rubella (for its effects on the embryo) and epidemic parotitis (bilateral dacrioadenitis). Relatively new in this chapter of ophthalmology is epidemic keratoconjunctivitis which Bietti saw for the first time in Italy in the island of Sardinia in 1943. Treatment is based mainly on the early use of antiseptics and caustics, antibiotics and convalescent's serum. Other

ocular manifestations of virus origin are those related to the so-called pharyngo-conjunctival fever caused by the type 3 adenoid-pharyngo-conjunctival virus (APC-3 type). The conjunctivitis is of follicular type with scarce serous secretion. There are no corneal complications or residual cicatrices. The ocular nervous system may be affected during the course of systemic disease by the virus of various epidemic encephalites, that of poliomyelitis, lymphocytic choriomeningitis and rabies. At times there may be such monosymptomatic manifestations of these virus diseases as ocular paralysis and optic neuritis. Viruses proper of animal pathology may also become localized in the eyes. Thus the virus of epizootic aphthae may in exceptional cases cause alterations of the vesicular corneoconjunctival type, whereas that of Newcastle's disease or of pseudo fowl plague may cause acute conjunctivitis often accompanied by transitory general manifestations. Conjunctival, less often corneal, lesions can follow the appearance of molluscum contagiosum and verruca vulgaris on the eyelids. Other virus diseases that may, sometimes very early, present ocular symptoms are yellow fever, dengue, Rift-Valley fever, and Rocky Mountain spotted fever. Particular mention should be made of ocular manifestations of rickettsioses, especially important for the ophthalmologist because it is believed that these can cause autonomous ocular manifestations. The hypothesis was advanced recently that a virus or a rickettsial condition may be the causative agent of sympathetic ophthalmia; studies to test this hypothesis are in progress. A possible viral etiology has been considered for pemphygus as well as for the syndromes of Reiter, Behçet, and Stevens-Johnson and for those of Harada and Vogt-Koyanagi. Studies are still in course to prove the viral etiology of benign lymphogranulomatosis (Besner-Boeck-Schaumann disease) and malignant lymphogranulomatosis (Hodgkin's disease) as well as of optic neuromyelitis and multiple sclerosis. This is a field rich with possibilities for research studies which may lead, it is hoped, to the solution of the many complex problems of ocular virology.

Comment: This is an interesting review of virus conditions although there is nothing particularly new discussed. Despite the problem of trachoma as an endemic disease in many portions of the globe there are many ophthalmologists in the United States who have never seen an active case. Through the efforts of the United Nations whole populations are now being treated prophylactically with sulfonamides and the disease is being eliminated in large areas, although it is probably still the chief cause of blindness in the world today.

A virus agent is considered the etiologic factor in a number of conditions characterized only by the absence of an obvious cause and the ineffectiveness of the usual forms of therapy. A most fruitful return could be expected by careful study of these conditions—Vogt-Koyanagi disease, Reiter's disease, Behçet's disease etc.,—by a competent virologist with the necessary laboratory facilities. Perhaps now that so many studies dealing with poliomyelitis have been completed, attention may be turned to these ocular conditions.

OPTICS

ROD AND CONE VISION IN RETINITIS PIGMENTOSA

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A strongly hereditary character, slow progressive course, and high incidence combine to make retinitis pigmentosa one of the most serious of ophthalmic problems. The two main symptoms are an early history of night blindness and a subsequent progressive loss of peripheral fields leading eventually to so-called gun-barrel vision and its attendant visual incapacity. The ophthalmoscopic picture of bone corpuscle-shaped deposits of black pigment in the retina is characteristic. On occasion, no pigment deposits are found (so-called retinitis pigmentosa sine pigmento). There may also be some narrowing in the caliber of the retinal arterioles. Both eyes are usually involved equally.

At present, there are two main methods of following the course of the disease. The less reliable is to observe changes in the appearance of the fundus. A slightly better gauge is obtained by checking by perimetry the narrowing of visual fields. The first method is wholly qualitative; the second yields only an arbitrary outer boundary of the residual functional retina with no information regarding the state of affairs within the boundary. On the whole, little is known about which of the visual cells, whether rods or cones, are the first to suffer attack or about the further course of the degeneration. Cogan (Tr. Am. Acad. Ophth., 1950) found that the rod and cone layer had disappeared entirely in all his cases except occasionally for a few abnormal cones in the central area and in the far periphery.

Several attempts have been made in recent years to analyze more closely the loss of visual capacities in retinitis pigmentosa. In the present investigation, an effort has been made through measurements of visual threshold and adaptation in normal persons and persons with early and late retinitis pigmentosa to establish quantitatively the functional status of rod and cone vision in the surviving retina. A special perimetric adaptometer was designed, and a procedure employed which singles out the thresholds of rod and cone vision in any desired area of the retina within 40 degrees from the fixation point. Thresholds were measured alternately in blue and orange lights, so chosen that in cone vision the threshold for blue lay above that for orange, and in rod vision well below that for orange. In this way one could specify unequivocally rod or cone function, or any mixture of the two. Visual thresholds, measured across various meridians of the dark-adapted retina, yield cross-sections (profiles) of rod and cone function

within the areas of measurement. In normal persons such profiles form a peak at the fovea, descending rapidly toward the periphery. The thresholds also shift from cones to rods in a transition zone 0.5 to 2.0 degrees around the fixation center. In the patients with retinitis pigmentosa the profile is inverted, the foveal thresholds forming a minimum. Associated with this change, there is a great deterioration of rod vision, most pronounced and earliest in the region within 25 degrees of the fovea, eventually also more peripherally. Cone vision also deteriorates peripherally, though much more slowly; it may appear normal in the fovea and immediate parafovea even in advanced stages of the disease, when gun-barrel vision alone is present. Pigmentation of the retina is apparent only after visual function has declined greatly.

Retinitis pigmentosa has long been known to involve hereditary factors, but its inheritance follows no simple pattern; cases have been described in which it appears dominant, recessive, or sex-linked recessive. Three of the subjects in this study, two brothers and a sister, aged 21, 24, and 18 years, were siblings. All three exhibited a remarkably similar pattern of retinal degeneration, although only two had had a diagnosis of retinitis pigmentosa; the other had no clinical history of the disease. The condition in these persons was apparently due to a dominant trait. The patterns presented by the two brothers were so nearly identical as to be easily confused, and that of the sister, though less advanced, was strikingly similar. The retinal profiles in these cases are almost like a family signature.

Although rod vision deteriorates more rapidly than cone vision in retinitis pigmentosa, there is apparently a wide latitude in the difference in rate between them. One of the subjects, for example, presented an atypical picture with normal cone vision over the whole retina, though rod vision had deteriorated completely. Whatever mechanisms are invoked to explain the origin of retinitis pigmentosa must attempt to account for great differences in the susceptibilities of rods and cones. The suggestion has been made that retinitis pigmentosa is connected with some local failure in the supply of or in the ability to use vitamin A. It has lately been shown that both rod and cone vision depend upon a specific *cis* isomer of vitamin A, called neo-b. This has a hindered *cis* configuration and probably always requires special conditions for its formation. The neo-b isomer of vitamin A has so far been identified only in eye tissues, where an enzyme has also been found that assists in its formation. None has been found in livers or in mammalian blood plasma. A condition might, therefore, exist in which the general supply of vitamin A to the organism and its general metabolism would be wholly adequate, and yet a failure to form this specific isomer might result in visual failure. Differences in the rate of synthesis between the rod and cone pigments might also operate in such a way that the cones could maintain their function relatively unimpaired under conditions in which rod function had virtually ceased. As for a possible relationship between vitamin A deficiency and the anatomic degeneration of the rods and cones, it may be pointed out that rhodopsin is an important element of structure in the outer segment of a rod. Rod opsin was recently found to be stabilized by its attachment to retinene, as in rhodopsin. If the supply of

neo-b retinene were to fail, so that opsin could not form rhodopsin, it is probable that opsin itself would soon deteriorate and with it the structure of the outer segments of the rods. The cones are in a different position. The rapidity with which cone opsin couples with neo-b retinene makes it certain that under deficiency conditions the cones will capture whatever neo-b vitamin A remains available. In addition, cone visual pigments, being much more dilute than those of the rods, play a proportionately smaller structural role. For both reasons, then, the cones might be expected to survive functionally and anatomically after the rods had failed.

All of this is still relatively unsupported hypothesis, but it is to be hoped that the growing knowledge of retinal structure and biochemistry, together with methods of observation such as those described, will lead to an increased understanding of the causes of retinitis pigmentosa.

Comment: This is certainly one of the most important papers read at the 1956 meeting of the Association for Research in Ophthalmology. It is an encouraging example of the eventual usefulness of the tools and results of basic research in the clinical field. Professor Wald is one of the greatest living experts on the physical and chemical basis of the visual process. Some years ago, in a contribution with Burian, he applied the research tools of retinal psychophysics to the study of amblyopia ex anopsia. In the present paper he and his collaborator, Dr. Zeavin, offer the first set of exact data toward an understanding of one of the most tragic and one of the most baffling diseases of the visual system.

The perimeter adaptometer presented in this study can be expected to become a standard tool not only of basic but also of clinical research in the field of visual psychophysics. The same can be expected of the new method of separating data of rod and cone sensitivity by the simple expediency of differential filters. But there is even more to this presentation.

Modern biologic research makes it more and more clear that the genetic transmission of normal and pathologic traits is, in essence, an enzyme transaction. Studies from Wald's laboratory make it appear that an especial form of Vitamin A (its so-called neo-*b*-isomer) and an especial enzyme (retinene isomerase) are needed for the providing of rods and cones with the appropriate compound protein essential for their healthy structure and proper functioning. Pigment degeneration of the retina is a hereditary, gene-bound and gene-transmitted disease. Our authors thus are certainly justified in assuming that the genetic failure of just this highly specific enzymatic transaction is the essence of the disease process.

Here again, this presentation proves that highly theoretic concepts, like those of modern genetics, can and do have direct bearing not only on our understanding but possibly even upon our therapeutic handling of a clinical entity in the treatment of which the clinician's hands were up to now all but bound in nihilism.

This admirable study needs really no comment, and even the best abstract cannot do full justice to its contents. No reader should miss the excellent contributions of Drs. Falls and Burian, offered in *Discussion* at the end of this paper.

ARTHUR LINKSZ

A QUANTITATIVE ANALYSIS OF THE HORIZONTAL MOVEMENTS OF THE EYES IN THE EXPERIMENT OF JOHANNES MUELLER

I. Methods and Results

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I. Methods

The manner in which variation in the dioptric power of each eye in far-to-near focus (accommodation) is related to the relative position of the lines of sight of the two eyes (convergence) has been a subject of controversy for many years. Johannes Mueller was the first (1826) to provide objective evidence that these two functions are related. Mueller noted that if one eye was occluded and the other eye changed fixation from a far to a new object along the same line of sight, the occluded eye moved nasalward.

Even with the definitive photographic data of Allen obtained at two different accommodative stimulus levels, there is still a dearth of information as to the time characteristic patterns of the change in accommodative convergence following the onset of far-to-near change in focus, and the way these patterns change with a change in the stimulus to accommodation. It seemed important, therefore, in order to gain a better understanding of Mueller's experiment in particular, and of the interrelation of accommodation and accommodative convergence in general, to repeat the original experiment at a variety of different accommodation stimulus levels in such a way that a quantitative analysis of the horizontal eye movements during the change in fixation from far to near could be formulated. Measurements of the way in which the eyes move when fixation is changed from a far to a near target along the same line of sight when the other eye is occluded were therefore obtained, using the ocular rotational potential. The absence of any large discontinuities in the curves derived by plotting the data suggests that the far-to-near change in focus occurs as a smooth continuous inward rotation of the occluded eye. This fact is important, because in these experiments two factors operate together, each of which may independently influence the amount of inward rotation of the eye. These are (1) the degree the test target is out of focus and (2) the near position of the test target. The absence of sharp discontinuities in the eye movement curves seems to show that in the present experiment either the proximity factor made no major contribution to the position of the eyes during the movement or the time characteristics of the two types of movements are identical.

Only the occluded eye was found to move, but the really surprising fact is not

that the movement of the fixating eye is damped, but the way in which the damping takes place. According to the usual testbook description, the fixating eye should make a saccadic movement to the right (when it is the right eye) and then the convergence movement should be completed as a yoked binocular act —the amplitude of the movements of each eye being identical. The present findings show that this is not what happens in Mueller's experiment. Apparently, in the authors' subject at least, the eye movements in Mueller's experiment follow the principle of least muscular effort established in another connection by Wundt. In binocular far-to-near focus, however, or in prism vergence testing, the eyes move (at least in a qualitative way) according to Haring's law of equal innervation of the ocular muscles of the two eyes. This variance implies that if Hering's law of equal innervation remains valid, then the way in which the yoked movements are damped in binocular asymmetrical convergence is essentially different from the way the yoked movements of the fixating eyes are damped in Mueller's experiment. One possible way in which this difference can be accounted for is that vergence movements (such as those in Mueller's experiment) are produced by innervation from the autonomic nervous system, while saccadic movements are produced by innervation from the somatic nervous system. In Mueller's experiment, the somatic system predominates and the fixating eye fails to move, but when fixation is binocular, the conditions are changed because the shift from far to near is associated with a change in fixation signal (in terms of the retinal feedback from the left eye in this particular experiment) as well as an accommodation signal. As a result, the fixation movement (mediated by the rapidly acting somatic nervous system) forces an irrelevant movement of the right eye, which the slower acting autonomic activity is not able to damp immediately. The magnitude of this irrelevant movement is apparently just large enough to cause the inward rotation of the eyes associated with the accommodation to be evenly distributed in the two eyes and to return the right eye to the starting point. It will be interesting to see if such speculations as these can withstand the test of future experiments.

II. Effects of Variation in Target Separation

In a further analysis of the horizontal movements of the eyes in the experiment of Johannes Mueller, the authors studied the way in which the various characteristics of the movement change with a change in the separation of the far and near targets. Generally speaking, the amplitude, average velocity, and average acceleration for both far-to-near and near-to-far types of movement show the same characteristic changes as the target separation increases. These changes are (1) an increase in amplitude, up to a certain maximum beyond which no further increase takes place, (2) an increase in the average (as well as the maximum) velocity of the movement, also to a certain maximum; and (3) an increase in the average (negative) acceleration of the target up to a difference in the stimulus to accommodation of 6 diopters, after which increasing target separation fails to increase the average acceleration. These findings, which show that two movements of equal amplitude are not necessarily similar, emphasize

the importance of studying as many features of the movement as possible. It now seems important to learn whether such changes in velocity and acceleration without changes in amplitude are associated with changes in the response as well as in the stimulus to accommodation.

Study of the time characteristics, which showed that the duration of the movement increased but slightly as the amplitude increased, while on the other hand both the average velocity and the average acceleration increased considerably as the amplitude increased, tends to support the hypothesis that the eye movement in Mueller's experiment is mediated through the autonomic nervous system and its more slowly responding components rather than through the more rapid somatic system.

Comment: The fundamental electromyographic studies of Breinin, (Arch. Ophth., 1955, *54:* 407) on the extraocular muscles have again turned attention toward the behavior of the eyes during asymmetric convergence and the problem of the applicability to their unequal rotations of Hering's law of equal innervation. The extremely interesting and well presented paper by Alpern and Ellen deals with the same problem. Our authors, with modern equipment, repeated one of the earlier psychophysiologic experiments by the great Johannes Mueller. They confirmed the finding that while one eye is made to accommodate by having it change fixation from a far to a near target which are both placed along the same line of direction, this eye, which fixates, remains motionless while the other eye, which is occluded, turns nasalward. This nasalward turn was smooth and continuous and there is no way of separating in its tracing an accommodative from a proximal convergence impulse—in case the latter at all exists. The training of the fixating eye proved that this eye did not move—at least it did not move as long as the other eye was occluded. The eye aligned with the distant and near target did not, however, remain motionless in a modification of the Mueller experiment, the case in which fixation was binocular, since no occluder was used. It looked in this case as if Bielschowsky's well-known interpretation would be valid and Hering's law vindicated. The tracing, thus, showed the aligned eye making "irrelevant" to-and-fro motions—as if opposing vergence and version innervations were making each other ineffective in the manner suggested by Bielschowsky. Similar "irrelevant" eye motions, adding up to zero displacement, were found in the tracing of one eye, whenever a prism was dropped before the other eye.

Our authors offer two possible explanations for this dissimilar behavior of the aligned eye under the two seemingly similar experimental set-ups. The second of them is especially interesting and expressed in the terms which muscle-physiology has recently borrowed from communication theory. This explanation also refers to work by one of the authors (not yet published) in which it is proposed that vergence movements (as called for in the original Mueller experiment) are mediated through innervation from the autonomous nervous system while saccadic movements (also called for in the modified experiment) are produced by innervation through somatic nerve channels. One will expect this work with interest and will be anxious to have further verification of the anatomic study which lies behind it.

ARTHUR LINKSZ

Classics of Ophthalmology
JAMES E. LEBENSOHN, *Editor*

ON SEMI-DECUSSATION OF THE OPTIC NERVES

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London

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The subject of my inquiry relates solely to the course by which impressions from images perfectly formed are conveyed to the sensorium, and to that structure and distribution of the optic nerves on which the communication of these impressions depends.

Without pretending to detect by manual dexterity as an anatomist, the very delicate conformation of the nerves of vision, I have been led, by the casual observation of a few instances of diseased vision, to draw some inferences respecting the texture of that part which has been called the decussation of the optic nerves, upon which I feel myself warranted to speak with some confidence.

It is well known that in the human brain these nerves, after passing forward to a short distance from their origin in the thalami nervorum opticorum, unite together, and are, to appearance, completely incorporated; and that from this point of union proceed two nerves, one to the right, the other to the left, eye.

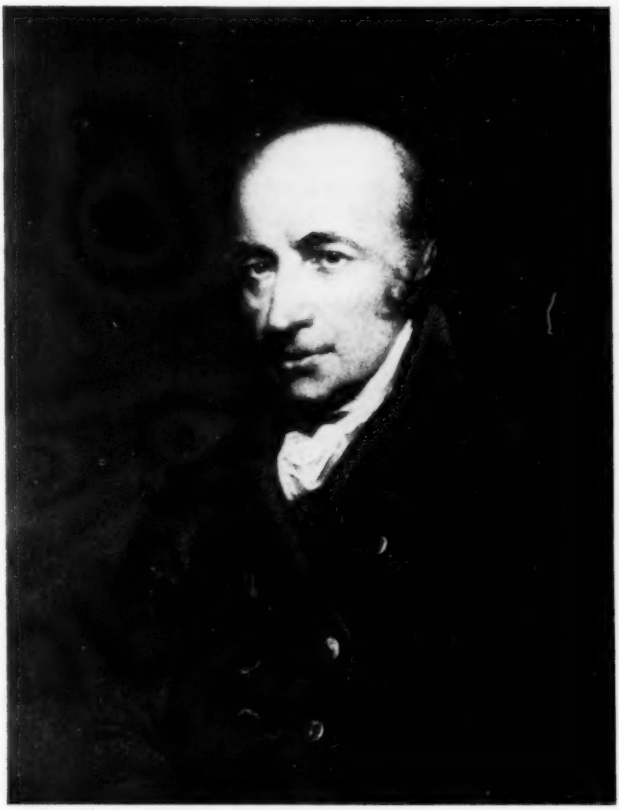
The term decussation was applied to this united portion, under the supposition that, though the fibers do intermix, they still continue onward in their original direction, and that those from the right side cross over wholly to supply the left eye, while the right eye is supplied entirely from fibers arising from the left thalamus.

In this opinion, anatomists have felt themselves confirmed by the result of their examination of other animals, and especially that of several species of fish, in which it is distinctly seen that the nerves do actually cross each other as a pair of separate cords, lying in contact at their crossing, but without any intermixture of their fibers.

In these cases it is most indisputably true, that the eye upon the right side of the animal does receive its optic nerve from the left side of the brain, while that of the left eye comes from the right side; but it is not a just inference to suppose the same continuity preserved in other animals, where such complete separation of the entire nerves is not found.

On the contrary, not only do I see reason, from a species of blindness which has happened to myself more than once, to conclude that a different distribution of nerves takes place in us, but I think my opinion supported by this evident difference of structure in fishes.

It is now more than 20 years since I was first affected with the peculiar state



DR. W. H. WOLLASTON
From an oil-painting in the possession of the Royal Society

of vision, to which I allude, in consequence of violent exercise I had taken for two or three hours before. I suddenly found that I could see only half the face of a man I met; and it was the same with respect to every object I looked at. In attempting to read the name JOHNSON, over a door, I saw only "SON"; the beginning of the name being wholly obliterated to my view. In this instance the loss of sight was toward my left, and was the same whether I looked with the right eye or the left. This blindness was not so complete as to amount of absolute blackness, but was a shaded darkness without definite outline. The complaint was of short duration, and in about a quarter of an hour might be said to be wholly gone, having receded with a gradual motion from the center of vision obliquely upward to the left.

Since this defect arose from overfatigue, a cause common to many other nervous affections, I saw no reason to apprehend any return of it, and it passed

away without need of remedy, without any further explanation, and without my drawing any useful inference from it.

It is now about 15 months since a similar affection occurred again, without my being able to assign any cause whatever or to connect it with any previous or subsequent indisposition. The blindness was first observed, as before, in looking at the face of a person, whose left eye was obliterated to my sight. My blindness was in this instance the reverse of the former, being to the right (instead of to the left) of the spot to which my eyes were directed; so that I have no reason to suppose it in any manner connected with the former affection.

The new punctum cecum was situated alike in both eyes, and at an angle of about three degrees from the center; for, when any object was viewed at the distance of about five yards, the point not seen was about 10 inches distant from the point actually looked at.

On this occasion the affection, after having lasted with little alteration for about 20 minutes, was removed suddenly and entirely by the excitement of agreeable news respecting the safe arrival of a friend from a very hazardous enterprise.

In reflecting upon this subject, a certain arrangement of the optic nerves has suggested itself to me, which appears to afford a very probable interpretation of a set of facts, which are not consistent with the generally received hypothesis of the decussation of the optic nerves.

Since the corresponding points of the two eyes sympathize in disease, their sympathy is evidently from structure and not from mere habit of feeling together, as might be inferred, if reference were had to the reception of ordinary impressions alone. Any two corresponding points must be supplied with a pair of filaments from the same nerve, and the seat of a disease in which similar parts of both eyes are affected must be considered as situated at a distance from the eyes at some place in the course of the nerves where these filaments are still united, and probably in one or the other thalamus nervorum opticorum.

It is plain that the cord, which comes finally to either eye under the name of optic nerve, must be regarded as consisting of two portions, one half from the right thalamus and the other from the left thalamus nervorum opticorum.

According to this supposition, decussation will take place only between the adjacent halves of the two nerves. That portion of nerve which proceeds from the right thalamus to the right side of the right eye, passes to its destination without interference; and in a similar manner the left thalamus will supply the left side of the left eye with one part of its fibers, while the remaining halves of both nerves, in passing over to the eyes of the opposite sides must intersect each other, either with or without intermixture of their fibers.

Now, if we consider rightly the facts discovered by comparative anatomy in fish, we shall find that the crossing of their entire nerves to the opposite eyes is in perfect conformity to this view of the arrangement of the human optic nerves. The relative position of the eyes to each other in the sturgeon is so exactly back to back, on opposite sides of the head, that they can hardly see the same object; they can have no points which generally receive the same impressions as we do; there are no corresponding points of vision requiring to be supplied with fibers

from the same nerve. In this animal, an injury to the left thalamus might be expected to occasion entire blindness of the right eye alone, and want of perception of objects placed on that side. In ourselves, a similar injury to the left thalamus would occasion blindness (as before) to all objects situated to our right, owing to insensibility of the left half of the retina of both eyes.

A disorder that has occurred within my own knowledge in the case of a friend, seems fully to confirm this reasoning, as far as a single instance can be depended upon. After he had suffered severe pain, for some days, about the left temple and toward the back of the left eye, his vision became considerably impaired, attended with other symptoms indicating a slight compression on the brain.

It was not until after the lapse of three or four weeks that I saw him, and found that, in addition to other affections which need not here be enumerated, he labored under a defect of sight similar to my own, but more extensive, and it has unfortunately been far more permanent. In this case the blindness was at that time, and still is, entire, with reference to all objects situated to the right of his center of view. Fortunately, the field of his vision is sufficient for writing perfectly. He sees what he writes, and the pen with which he writes, but not the hand that moves the pen. This affection is, as far as can be observed, the same in both eyes, and consists in an insensibility of the retina on the left side of each eye. It seems most probable, that some effusion took place at the time of the original pain on that side of the head, and has left a permanent compression on the left thalamus. This partial blindness has now lasted so long without sensible amendment, as to make it very doubtful when my friend may recover the complete perception of objects on that side of him.

In reviewing the several phenomena that I have described, we find partial blindness occurring at the same time in both eyes. This sympathy from disease is readily explained, on the supposition that the parts which sympathize receive their nerves from the same source, while the opposite halves of the eyes, which are not at the same time similarly affected, are supplied from an opposite source; and the inference is immediate, that in common vision also the sympathy of corresponding points, which receive similar impressions from the same object, is dependent on the arrangement of nerves thus detected by disease.

We find, moreover, in the sturgeon (and it is the same in some other fish) whose eyes can scarcely see the same object at once and have no corresponding points which ordinarily sympathize, that the two eyes do not receive any nervous fibers from the same source; but one eye receives its nerve wholly from one side, and the other from the other side of the brain.

From the structure of these fish we learn distinctly, that the perception of objects toward one side is dependent on nerves derived from the opposite side of the brain; and in the last case of diseased vision above related, we find apparent injury to one side of the brain, followed by blindness toward the opposite side of the point to which both eyes are directed.

A series of evidence in such apparent harmony throughout, seems clearly to establish that distribution of nerves I have endeavored to describe, which may be called the semi-decussation of the optic nerves.

It may perhaps to some person appear surprising, that so many as three in-

stances of a disorder which they presume to be rare, should have been witnessed by one individual; but I apprehend, on the contrary, this half-blindness to be far more common than is generally supposed; and I might with as much reason express surprise at its having so far escaped notice, were I not aware of how many facts commonly remain disregarded, merely for want of explanation. It is evident that I once, and for a long time, overlooked the inference that is to be drawn from this affection; and if the disorder had not happened to me a second time, I might never have reconsidered its cause.

Even since the preceding pages were written, I have met with two more cases of this disease. One of my friends has been habitually subject to it for sixteen or seventeen years, whenever his stomach is in any considerable degree deranged. In him the blindness has been invariably to the right of the center of vision, and, from want of due consideration, had been considered as temporary insensibility of the right eye; but he is now satisfied that this is not really the case, but that both eyes have been similarly affected with half-blindness. This symptom of his indigestion usually lasts about a quarter or an hour or twenty minutes, and then subsides, without leaving any permanent imperfection of sight.

I have not seen the subject of the fifth case, but I am informed that he has had many returns of this affection, generally attended with headache, and always lasting about twenty minutes, with very little variation.

Comment: Isaac Newton in the first edition of OPTICKS (1704) first formulated the hypothesis of semi-decussation. The hemianopsia accompanying the migraine to which Newton was subject very probably suggested the concept. In 1723, Vater and Heinicke (cited by Mackenzie) described several clinical cases of hemianopsia for which an explanation by Newton's hypothesis was offered. Chevalier Taylor also adopted this view and contributed a drawing clearly illustrating this assumption (*The Mechanism, or New Treatise of the Anatomy of the Globe of the Eye*, 1738). After Wollaston revived the theory, the idea of semi-decussation received immediate acceptance and was popularized by the physiologist, Johann Müller; but a half-century later the question became a controversial issue. Though Gudden apparently had confirmed its occurrence by serial sections of the chiasma, Michel held that his personal studies indicated that the nerve fibers crossed completely. He argued that the semi-decussation theory could not account for binocular nasal hemianopsia on the basis of a single lesion and that only by assuming total decussation could all possible forms of hemianopsia be logically explained. Schoen countered that binasal hemianopsia, if it did exist, was extremely rare. Other champions of semi-decussation were von Graefe, Hirschberg, Knapp, Mauthner and Hughlings Jackson; and this viewpoint became definitely established by the authoritative studies of Cajal and the accumulation of postmortem evidence. Three years after Wollaston's paper on hemianopsia he noted an immobility of the right pupil and numbness of the left arm. At his death the following year an autopsy revealed that a tumor as large as a hen's egg had invaded the right optic thalamus. Considering the size of the lesion it is surprising that his intellect remained unclouded to the last. The tumor was evidently sufficiently slow-growing to permit for some time an adjustment of the nerve structures.

Biographical Note: William Hyde Wollaston (1766-1828) was the second of 17 children. His grand-uncle was the eminent Dr. William Heberden. After study in Cambridge and London, he graduated in medicine in 1793 but failed to win success as a practitioner. On

receiving a small legacy in 1800, he abondoned practice and zealously embarked on a career of independent investigation. From a process of purifying and welding platinum, he made $150,000 and incidentally discovered the elements, palladium and rhodium. His optical contributions include the determination of the refractive index by utilizing the critical angle, the discovery of the dark lines in the solar spectrum and of ultraviolet activity. The most noteworthy of his numerous inventions were the reflecting goniometer for the measurement of crystals, the doublet used as the objective of the compound microscope, the camera lucida, the double-image prism, and meniscus lenses. Other investigations contributed to astronomy, acoustics, mechanics, mineralogy and botany. The present British imperial gallon was standardized at his suggestion to that containing 10 pounds of distilled water at 62°F. After learning the fatal nature of his illness, he bequeathed his wealth for the promotion of research and spent his last months in completing unfinished scientific papers and experiments.

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Ophthalmic Meetings

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

The 61st annual meeting of the American Academy of Ophthalmology and Otolaryngology, under the presidency of Dr. Albert C. Furstenberg, chairman and professor of the department of otolaryngology and dean of the medical school, University of Michigan, was held at the Palmer House, Chicago, from October 14 to 19, 1956.

"A Look to the Future", was the title of the presidential address. The guest-of-honor, Dr. Frederick A. Coller, chairman and professor of the department of surgery, University of Michigan, spoke on the "Evolution of surgery and its specialties," which included a review of not only advances in major surgery but of the two specialties represented by the membership of the Academy.

Highlights of the scientific sessions on ophthalmology were the XIII Jackson Memorial Lecture on "The lens epithelium in the pathogenesis of cataract," by Dr. Ludwig von Sallmann, chief of ophthalmology, National Institutes of Health, Bethesda, Maryland; a symposium: "Postoperative cataract complications (pathogenesis, clinical manifestations, pathology and treatment)," given by Dr. Michael J. Hogan of San Francisco, Dr. John M. McLean of New York, and Dr. A. Edward Maumenee of Baltimore; and a symposium: "Accomodative esotropia," given by Dr. Kenneth C. Swan of Portland, Dr. Goodwin M. Breinin of New York, and Dr. Frank D. Costenbader of Washington.

The other papers offered a wide variety of interest. The authors gave outstanding presentations which were enhanced further by well selected and assigned discussers. These included, "The treatment of retinal detachment by vitreous implant," by Dr. Donald M. Shafer of New York, and discussed by Dr. Dohrmann K. Pischel of San Francisco and Dr. Graham Clark of New York; "The bulbar conjunctival lymphatics and their clinical significance," by Dr. H. Saul Sugar, Dr. Ahmed Riazi, and Dr. Rome Schaffner of Detroit, and discussed by Dr. Kenneth C. Swan of Portland and Dr. Karl W. Ascher of Cincinnati; "Preretinal and optic nerve-sheath hemorrhage," by Dr. Dale C. Smith, Dr. Thomas P. Kearns and Dr. George P. Sayre of Rochester, Minnesota, and discussed by Dr. Frank B. Walsh of Baltimore, and Dr. Windsor S. Davies of Detroit; "The role of stress in ocular disease," by Dr. Isaac S. Tassman of Philadelphia, and discussed by Dr. Harley E. Cluxton, Jr. of Chicago and Dr. David O. Harrington of San Francisco; "The treatment of retinoblastoma with radiation and T. E. M.," by Algernon B. Reese, *et al.* of New York, and discussed by Dr. William F. Hughes, Jr. of Chicago; "Penetrating wounds of the eye," by Dr. P. Robb McDonald of Philadelphia, and discussed by Dr. Murray F. McCaslin of Pittsburgh; "Estimation of loss of visual efficiency," by Dr. Edmund B. Spaeth of Philadelphia, and discussed by Attorney Percival E. Thompson of Chicago;

"Eye protection against small high speed missiles," by Dr. H. W. Rose and George M. Stewart of Randolph Field, Texas, and discussed by Dr. Arthur H. Keeney of Louisville; "The production of heterochromia and glaucoma by diffuse malignant melanoma of the iris," by Dr. Benjamin Rones and Dr. Lorenz E. Zimmerman of Washington, and discussed by Dr. Harvey E. Thorpe of Pittsburgh and Dr. Alexander R. Irvine, Jr. of Beverly Hills; "Early treatment of orbital fractures," by Dr. Byron Smith and Dr. John M. Converse of New York and discussed by Dr. Daniel F. Fisher of Memphis; "Bilateral anomalies of the oblique muscles," by Dr. Arthur Jampolsky of San Francisco and discussed by Dr. Hermann M. Burian of Iowa City, and Dr. William E. Krewson III of Philadelphia; "Malignant melanoma in the temporal periphery associated with macular symptoms as an initial finding," by Dr. Wilfred E. Fry and Dr. P. Robb McDonald of Philadelphia; and discussed by Dr. Bertha A. Klien of Chicago; "Use of the Harrington multiple pattern field screener in industry," by Dr. Logan T. Robertson of Asheville, and discussed by Dr. David O. Harrington of San Francisco; "Factors influencing the blood volume of the choroid and retina," by Dr. Jerome W. Bettman and Dr. Victor G. Fellows, Jr. of San Francisco and discussed by Dr. Irving H. Leopold of Philadelphia; and Dr. Arnall Patz of Baltimore.

The scientific papers were frequently alternated with movies, all of which were outstanding. These included "The scleral fold operation for retinal detachment," by Dr. William G. Everett and Jay G. Linn, Jr. of Pittsburgh; "Cataract extraction following filtering operation for glaucoma," by Dr. Harold G. Scheie of Philadelphia; "Modified orbital decompression," by Dr. William J. Knauer, Jr. of Jacksonville; "Scleral shortening: A new and simplified method of use in retinal detachment," by Dr. Daniel M. Rolett of New York; "Scleral support with metal rings in intraocular surgery," by Dr. G. Bonaccolto of New York; and "Exenteration of the orbit," by Dr. Algernon B. Reese of New York.

There were 26 scientific exhibits, 16 of which pertained to ophthalmology. Dr. David O. Harrington's exhibit, "Visual field interpretation," was awarded first prize; "Precancerous and cancerous melanosis of the conjunctiva," by Dr. Algernon B. Reese and Dr. Bradley R. Straatsma of New York, second; and "The effect of glaucoma operations upon aqueous dynamics," by Dr. Peter C. Kronfeld and Dr. H. Isabelle McGarry of Chicago, third.

The Council for 1957 is as follows: President, Erling W. Hansen of Minneapolis, Minnesota; president-elect, LeRoy A. Schall of Boston; first vice-president, Louis H. Clerf of St. Petersburg, Florida; second vice-president, David O. Harrington of San Francisco; third vice-president, Oliver E. Van Alyea of Chicago; past president, Walter H. Theobald of Chicago; past president, Algernon B. Reese of New York; past president, A. C. Furstenberg of Ann Arbor; executive secretary-treasurer, editor and business manager of the Transactions, William L. Benedict of Rochester, Minnesota; secretary for ophthalmology, Kenneth L. Roper of Chicago; secretary for otolaryngology, Eugene L. Derlacki of Chicago; secretary for instruction in ophthalmology, A. D. Ruedemann of Detroit; secretary for instruction in otolaryngology, and maxillofacial surgery,

Dean M. Lierle of Iowa City; secretary for Home Study Courses, Daniel Snydacker of Chicago; secretary for public relations, Glen G. Gibson of Philadelphia; councillors, Sam E. Roberts, Kansas City, Harold H. Joy, Syracuse, N. Y., William J. McNally, Montreal and Col. Victor A. Byrnes, (MC), U.S.A.F., Washington.

The next meeting of the Academy will be held at the Palmer House, Chicago, October 13–18, 1957. New Candidates elected to membership numbered 236.

KENNETH L. ROPER

Reports from Abroad

FRANCE

The Société Française d'Ophtalmologie held its 63rd Congress from the 6th to the 10th of May this year at Paris. As usual, this important meeting was very widely attended by ophthalmologists coming from most of the countries of Europe as well as from the New World.

The subject of the Report, which was presented this year by Professeur egrégé Bregeat of the Faculty of Medicine of Paris, was papillary edema. It was a very important study, presented in a volume of 900 pages richly illustrated, in which the author surveyed this great problem of ophthalmologic pathology, especially in its neurosurgical aspects.

Recent technical advances (retinophotography, study of the summations in the examination of the visual field, among others) made it possible for their author to provide information about the points he has been able to define in this very delicate field.

In addition to the Report, which was the subject of many discussions, the working sessions were devoted to other aspects of ophthalmology, notably the treatment of amblyopia and affections of the optic nerve.

As usual, showings of films dealing with ophthalmology and operative sessions in various Parisian hospitals completed this annual meeting.

The next Congress, which will be centered about the study of "biomicroscopy of the posterior vitreous and of the retina," to be carried out by Mme Schiff-Wertheimer and Busacca and Goldmann, will take place at Paris, at the Centre Mercelin-Berthelot, from May 12th to 16th, 1957.

Ophthalmologists who are not members of the Society may also take part in it, and undoubtedly this future Congress, by the importance of the report that is to be given before it, will be inscribed in the tradition of the brilliant congresses of the Société Française d'Ophtalmologie.

Guy Offret, Secretary-General
Société Française d'Ophtalmologie

GERMANY

The Annual Meeting of the German Ophthalmologic Society was held under the presidency of Professor Lindner in Heidelberg on September 3 to 6, 1956.

The large number of presentations (60 papers, 20 communications, 13 scientific exhibits and 4 motion pictures) makes it impossible to mention all of them. The reviewer can only select those which he thought most important.

At the first session various subjects of physiological optics were discussed. Besides papers on adaptation, visual field tests and aniseikonia, problems of conservative treatment of strabismus were discussed. Several papers on glaucoma followed. Rohen reported on anatomic studies of the angle of the anterior cham-

ber in man and animals, and emphasized the special position of the human chamber angle. Siegert investigated the cholesterol level and the total lipoid content of the blood serum in patients with glaucoma. He did not find any deviation from the normal valves, and the concept of a hyperthyroid metabolism in patients with glaucoma was refuted.

Van Beuningen reported on the present state of tonography. He made an attempt to avoid, with the aid of additional methods of examination, the difficulties which may often occur with the interpretation of tonographic results.

Rosengren reported on experiments with a perilimbic suction cap which increases the intraocular pressure. The rise of pressure recedes after 15 to 30 minutes in normal eyes, but persists for a longer time in glaucoma.

Hager observed the spontaneous ocular pressure for three days. With the aid of the pressure tracing he was able to decide whether or not conservative treatment offered a favorable prognosis.

Leydhecker, Dardenne and Helferich reported on experimental and clinical studies with combined miotics. They established that the inhibitory effect may be increased rather than impaired by the *simultaneous* application of reversible (neostigmine) and irreversible [paranitrophenol diethyl phosphate (Mintacol)] cholinesterase inhibitors.

Lindner reported on changes of the refraction value of concave lens when moved away from the eye. Hollwich and Cavka presented contributions to the surgical treatment of glaucoma.

H. K. Müller, Kleifeld, Hockwin and Dardenne gave four reports on the work done at the Ophthalmologic Clinic in Bonn with regard to metabolism in the lens. The clinically interesting result of these studies is the observation that pilocarpine and Mintacol, when administered in therapeutic concentration, influence the metabolism of the lens. The absorption of oxygen is particularly inhibited.

Schreck, Barthelmess, Walser and Dannheim reported on surgical treatment of cataract with insertion of an anterior chamber lens. In the discussion which followed the consensus was that the anterior chamber lens has less tendency to cause complications than the Ridley lens.

Ullerich and Podesta repeated the well-known experiments by Ricker, concerning the mechanics of stasis, on the conjunctiva of warm-blooded animals. It came as a surprise that Ricker's results could not be confirmed. Additional studies on cold-blooded animals showed that the development of peristasis and stasis does not depend primarily on the width of the vessels. The report was followed by a long and interesting discussion, since Ricker's findings and his "stage law" concerning the concept of inflammation, has been contested for the first time on the basis of extensive experiments.

Meyer-Schwickerath reported on 450 patients who were treated with light-coagulation. Particular emphasis was placed on the treatment of periphlebitis (Eal's disease), proliferating retinitis, angiomatosis retinae, small melanosarcomas, small gliomas, and Coats's retinitis. In addition, the method of prophylactic coagulation for the prevention of retinal detachment was improved.

Renky reported good results obtained with lamellar resection of scleras in patients with retinal detachment with an unfavorable prognosis.

W. Jaeger activated the fibrinolysin of the patient's own blood by injection of Pyrexal [a proprietary highly purified pyrogen obtained from Salmonella abortus equi (lipopolysaccharide) (Wander, Bern)] and achieved a rapid lysis of the intraocular fibrin.

Weigelin and Niesel studied the effect of vasodilators and vasoconstrictors in patients with headache. These studies were carried out with the aid of functional dynamometry devised by Weigelin. The result of this therapeutic test was used as a basis for continued therapy.

A diversified social program had been prepared as usual. A visit in a large chemical plant in the surroundings of Heidelberg was a most pleasant experience.

G. MEYER-SCHWICKERATH
University Eye Clinic, Bonn, Germany

Book Reviews

"Comparative Anatomy of the Eye," by Jack H. Prince (*Charles C Thomas, 418 pp., $8.50*), *is the first book in its field to appear in thirteen years. It is reviewed by Gordon L. Walls, who wrote "The Vertebrate Eye."*

By Gordon L. Walls

This should and could have been a very good book (for which there is a great need), but unfortunately it is not. Its trouble is not just that it is full of flaws, but that the only people who can recognize most of the flaws are those few who know the field so well they they don't need the book in the first place. A great many professional human-eye people who will buy it, to learn from it, will accept every statement; for they will not know which ones to reject.

The order in which the parts of the eye and major physiologic processes are taken up is logical. To this extent the organization of the book is excellent. In many chapters, the title leads one to expect certain things to be discussed, which instead are in the next chapter. The most jarring feature is a tremendous over-use of italics, and, rarely for emphasis and never for genus names (where it is mandatory under zoological rules), but for both the names of structures and the *common* names of animals and groups of animals.

The author has used group-names to embrace forms which are not all related, and to exclude from groups forms which really belong to them. Thus, *carnivores* means both the placentalian order Carnivora and those marsupials which happen to eat flesh. He speaks of the dolphins "emulating" the whales as if the dolphins were not whales themselves. Both *artiodactyls* and *ungulates* (without apology) are used, as if on equal footing, although the latter is an archaic name for an artificial group which includes the former. If one does not look up *iguana* in the glossary, one does not find out that the author is not talking about the familiar three-foot monsters of our zoos, but the tiny anoles of the West Indies. The armadillo may be an ant eater, but this does not make him an *anteater*.

The avoidance of scientific names in the text and in the figure captions forces any serious reader to keep his right thumb stuck into the book at page 385, so that he can fairly quickly look to see what animal the author is discussing. Any educated American knows what a copperhead is, but he can absorb a lot of information from the book about "the *copperhead*" without learning that the author is talking about an Australian relative of the cobra, not the American cousin of the rattlesnake. Similarly, the Amerind word opossum is corrupted to *possum*, and used for an Australian animal rather than for the dear halfwit we all know. And, what could *native cat* mean to an American? Surely nothing but the bobcat, not the obscure marsupial the author is talking about.

It is startling to come upon the statement that a circle is the least efficient shape a pupil can have. This is unexplained in this place in the text; and the average reader, using the book "for reference," may never happen to find out

what is meant by it. It is that most round pupils cannot close as far as most slit pupils. There are several exceptions but more important is the simple fact that if an animal, considering his way of life, can get along just fine with a round pupil, then this is what he will be found to have. Where is the "inefficiency" here? The author states that a contracted slit pupil always confers high visual acuity regardless of the makeup of the retina behind it, so that a pure-rod shark may see about as well as a pike.

There is a throng of plain and simple mis-statements of fact in the ten-page "Rapid Reference Table." The bowfin is a teleost. Teleosts have no scleral ossicles. Frogs, all birds, and turtles in general have foveas (absent in all frogs, domestic birds and the kiwi, and present in only one known turtle). Crocodiles and *Sphenodon* are lizards. *Sphenodon* has cone oil-droplets, and reptiles have a Crampton's muscle (a bird monopoly). Turtles have partially decussated optic nerves and birds very likely do also (no known case in either group). Some diurnal snakes lack double cones (no known case).

In accommodation in birds the lens is moved backwards and forwards (only fishes and snakes accommodate thus). Nocturnal birds are said to have no colored cone oil-droplets. The corneal substantia propria "consists of modified connective tissue and alternating lamellae of fibrous tissue." The contraction of the bird ciliary muscle somehow makes the ciliary processes exert *traction* (not pressure) on the lens. Since no teleost has both a falciform process and a choroid gland, one of these structures had to evolve from the other. The powder tapetum of the opossum is called a fibrosum, and birds are said to have a fibrosum (no known case of a tapetum lucidum of *any* kind). There is little doubt that all fishes have guanin tapeta (although such are known for only a few species out of hundreds studied). The retinal vessels in mammals supply the receptor layer. "The natural (?) shape for an eye is spherical"—even though only a few lissamphibians, snakes, and mammals (all, *terminal* groups) have spherical eyeballs.

The eyes of snails contain homologues of Bowman's membrane and (retinal) Müller fibers. (Incidentally, we are told that it is Bowman's membrane, rather than Descemet's, that provides important resistance to infection, etc.) Frontalization of the eyes is tied to diurnality (although the strongly frontalized primates include both nocturnal and diurnal forms, most squirrels and lizards are diurnal but never frontal, the most frontal of birds are the owls, and the most frontal of fishes are deep-sea dwellers).

The anatomical treatment of the retina spread through three chapters, is completely unreliable. The terms "double cone" and "twin cone" are used interchangeably. The distribution, reasonable phylogeny, and probable optics and physiology of the colored oil droplets are confused.

The brains of the organisms are just as queer as their eyes. The superior colliculus is "a rudimentary cortex" even though it is not in the cerebrum. And, the superior colliculus is in command of accommodation and pupil movements. The lateral geniculate nucleus sends fibers "to every cortical connection." In Man, it affords multiplication of paths and reciprocal overlap, and in mammals generally it transmits to the superior colliculus. The proportion of decussating opticus fibers

in Man is not ⅔ but ½. Almost every human optic-tract fiber goes to the lateral geniculae, and almost every uncrossed fiber arriving there synapses with a fiber to the colliculus. The human pineal gland is "popularly associated with growth and sexual development." Ninety per cent of the reptilian brain is concerned with olfaction; and, reptiles have partially decussated optic nerves (a large generalization to base upon one lizard and one snake). The publishers have lavished abundant cuts and their usual beautiful format, typography, presswork, paper, and binding on the book. It is just too bad that good bookmaking does not ensure good books.

Current Review

THE USE OF PLASTIC LENSES IN THE ANTERIOR CHAMBER

Indications—Technique—Personal Results*

Joaquin Barraquer

The Institute Barraquer, Barcelona, Spain

With the discovery of plastic materials, new therapeutic advances have been made in medicine and surgery. Ridley was a pioneer, indeed, when, in 1949, he inserted the first plastic lens in the retro-iris space after an extra-capsular cataract extraction. Phases of enthusiasm and skepticism have followed this procedure, but considering the merits and disadvantages of this operation, its value now appears to be restricted to those cases of mature monocular cataract which are not associated with glaucoma and which are not due to an inflammatory process. Even in these cases the functional results have not always been entirely satisfactory. Patients who obtained good vision soon after the operation were subsequently disappointed because of diminished visual acuity arising from opacification and wrinkling of the posterior capsule, or by loss of binocular function caused by the development of a slight myopia due to displacement of the plastic lens by retraction of the posterior capsule.

Although Ridley's operation is now almost obsolete, his name will always be remembered with honor and affection, as is the name of Gonin in the surgical treatment of retinal detachment.

In order to extend the use of plastic and to achieve better results, several ophthalmologists have developed a new type of lens which is placed in the anterior chamber. Credit for this development goes to Benedetto Strampelli of Rome who deserves our praise and gratitude, as he was the first ophthalmologist to achieve success in placing this type of lens in the anterior chamber. We have adopted his pattern of the acrylic lens with minor modifications and we are completely satisfied with the results which we have obtained.

INDICATIONS FOR THE ANTERIOR CHAMBER LENS

(1) *Aphakia*
- (a) Normal intra-capsular extraction
- (b) Normal extra-capsular extraction
- (c) Secondary cataract with posterior synechia
- (d) Aphakia with total iridectomy, even with prolapse of vitreous into the anterior chamber

* Reprinted by permission from the 1956 Transactions of the Ophthalmological Society of the United Kingdom.

(2) *Non-progressive high myopia*
   (a) Monocular, to correct anisometropia
   (b) Binocular, to improve visual efficiency

(3) *High hypermetropia.* Similar indications as in myopia. The greatest care is required with these patients because the anterior chamber is shallow.

TECHNIQUE

(1) *The plastic lens.* The lens is specially made for each case according to the individual's specifications, taking into consideration the refractive error and the diameter of anterior chamber.

   (a) *Refraction.* This must be done very accurately, both by skiascopy and subjective methods. The distance between the correcting lens and the vertex of the cornea must also be precisely measured.

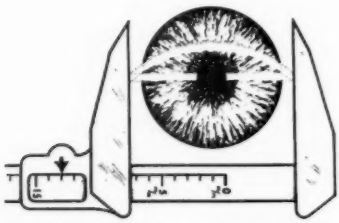

FIGURE 1. Measurement of diameter of the anterior chamber under slit-lamp for proper size of the lens.

   (b) *Diameter of the anterior chamber.* This measurement is obtained with a Vernier's scale under slit lamp examination (Fig. 1). In doubtful cases two lenses are ordered, with 0.5 mm. difference in length in order to select the proper one at the time of the operation.

The specialized optician can make the lens with this data, i.e., the refractive power, the distance between the cornea and the correcting lenses set in the frame, and the diameter of the anterior chamber. The radius of curvature of the non-optical part of the lens is 14 mm. A smaller radius makes the plastic lens too curved and complicates its introduction into the anterior chamber. Additionally, the corneal endothelium may be injured. A greater radius of curvature makes the lens too flat so that it will be in contact with the iris, especially in non-aphakic patients where the crystalline lens is "*in situ.*" It is advisable to examine the plastic lens under the slit lamp for any scratches or other defects of manufacture before operation.

The plastic lens is sterilized with soap and water and then put into one per cent solution of Armil (alkil-cetil-dimethyl-benzyl-ammonium). A few seconds before the insertion it is washed with absolute alcohol to eliminate any greasy film which might cover and blur transparency without danger of any chemical action on the acrylic substance.

FIG. 2

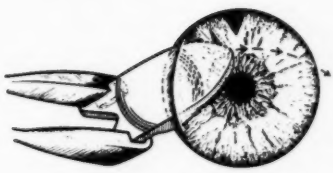

FIG. 3

FIGURE 2. Special forceps, the ends of which have a groove or canal to adapt to the width of the lens.

FIGURE 3. Insertion of the lens in the anterior chamber avoiding the pupillary area.

(2) *Instruments*

No special instruments are required but we have designed a pair of forceps (Fig. 2) which facilitates insertion.

(3) *Operation*

(a) *Inclusion in an eye which has been operated on by phacoerysis intracapsular extraction*)

This is performed two or three months after the cataract extraction when the refraction is fully stabilized.

(*1*) The patient must be under pharmacodynamic potentialization which produces a general relaxation and ocular hypotony; topical anaesthesia with a ten per cent solution of cocaine is then the only anesthetic required.

(*2*) The pupil must be miotic in order to avoid a prolapse of the vitreous in the anterior chamber.

(*3*) Fixation of the superior rectus muscle is essential.

(*4*) The corneal incision is made with a keratome and enlarged with Westcott's scissors. The incision must be wide enough to admit the lens without any difficulty (Fig. 3). It must be entirely corneal so that the extremities of the lens, once put in place, are not in contact with the incision. (Fig. 4 & 5) The incision must be made without any pressure upon the globe, and that is why keratome and scissors are preferred in these cases.

(*5*) The lens should be inserted without exerting any pressure on the eyeball or injuring the corneal endothelium. It must be gradually and gently slid into the anterior chamber away from the sphincter pupillae without hooking the pupil with this maneuver. When the proximal end of the lens is almost at the angle of the anterior

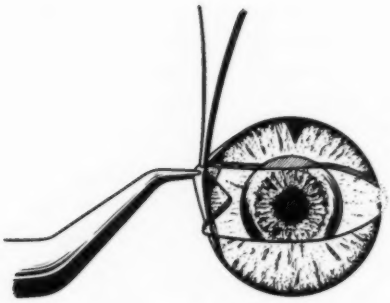

FIG. 4

FIG. 5

FIGURE 4. *Upper.* Slight traction on the scleral lip of the wound (with little pressure on the caudal ends of the lens) completes its introduction.

FIGURE 5. *Middle.* Lens in proper position with ends resting in the angle without coming in contact with the wound.

chamber a little pressure over both caudal ends accompanied by gentle traction of the scleral flap (Fig. 4) will be enough to bring the lens into the correct position with its three ends resting in the chamber's angle (Fig. 5). We leave the lens in a horizontal position for the following reasons:

(*a*) Introduction is easier in this position

(*b*) Movement of the lids to not produce displacement

(*c*) The lens is less visible

(*d*) There is no danger of blocking the peripheral iridectomy by the resting tips of the lens, which is possible if the lens is in vertical position.

(*6*) The incision is closed with two or three corneal sutures (natural virgin silk). The incision is widely separated from the lens and there is no danger of reopening the wound.

(*7*) The anterior chamber is irrigated with acetylcholine solution if additional miosis is required.

(*8*) Air is injected into the anterior chamber if the iris has a tendency to pass in front of the lens. (These latter two steps are not required in the majority of cases.)

(b) *Inclusion in an eye after the extra-capsular operation*

(*1*) If the peripheral iridectomy has not been performed it must be done at the time the lens is inserted.

(*2*) If the posterior capsule is intact a supero-temporal incision is made with a cataract knife (there is no danger of prolapse of vitreous), and a peripheral iridectomy performed at the 12 o'clock position. Miosis is useful because it facilitates the introduction of the lens but it is not as essential as after an intra-capsular extraction.

(*3*) When there is secondary cataract, capsulotomy should not be done immediately. It is wise to wait for ten or fifteen days, and similarly, if there are posterior synechiae causing an updrawn or hammock of the pupil a small iridotomy can be performed along with the capsulotomy. The technique is easier than it looks. After small incision with a keratome needle, we introduce Weeker's scissors underneath the lens and cut the posterior capsule.

(*4*) If the posterior capsule has already been divided the technique of the operation should be identical to that used after phacoerysis.

(c) *Inclusion in eyes with total iridectomy.* Generally, these are traumatic cases, due to perforating injuries, where it has been necessary to perform a total iridectomy. An acrylic lens may be placed perpendicularly to the iridectomy. In this way it will have a good support and the same security as in a normal eye.

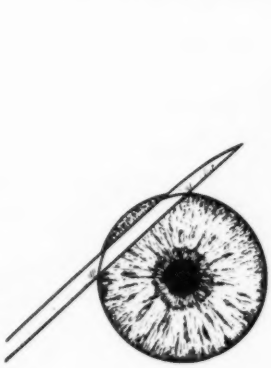

FIG. 6

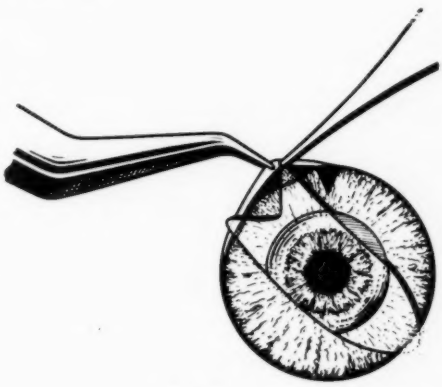

FIG. 7

FIGURE 6. *Lower.* In non-aphakic cases, the incision must be slightly larger in order to permit the entry of the lens easily and facilitate making small peripheral iridectomy.

FIGURE 7. *Upper.* The lens is slightly rotated to bring it into horizontal position.

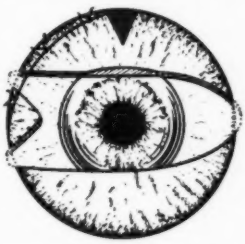

FIG. 8

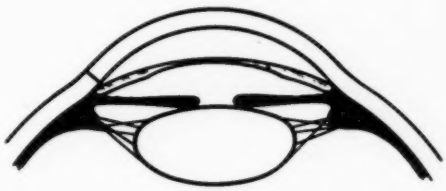

FIG. 9

FIGURE 8. *Middle.* Lens is in perfect normal horizontal position.

FIGURE 9. *Lower.* Negative lens for myopic patients in correct position

(d) *Inclusion in eyes with vitreous humor in the anterior chamber.*
(*1*) Hypotony is of the utmost importance in these cases.
(*2*) The conjunctiva is dissected at the limbus in order to have a conjunctival flap for covering the wound (possible loss of vitreous).
(*3*) "Ab externo" corneal incision with a keratome needle or razor blade, enlarged with Westcott scissors.
(*4*) Insertion of the lens.
(*5*) If there is any vitreous loss it should be cut with scissors at the edges of the wound.
(*6*) Corneal suture with conjunctival covering.
(*7*) Air injection in the anterior chamber.

(e) *Inclusion in non-aphakic eyes.*
(*1*) A wide incision in supero-temporal quadrant. (In the right eye, from 8 to 1, and in the left eye from 11 to 4 o'clock position. See figure 6.)
(*2*) Small peripheral (basal) iridectomy, being certain that the pigment layer of the iris is not left intact.
(*3*) Placement of the lens in a horizontal position. (Figs. 7, 8, 9).

INCIDENTS

(1) *Imperfect dimension of the lens.* The lens may be too small or too large. If it is too large it produces deviation of the pupil, hypotony (small cyclodialysis) and pigmentary precipitates which disappear very slowly. In addition, the insertion of the lend is difficult and surgical trauma is greater. Small lenses change position with the eye movements—this represents permanent micro-trauma on the iris which must be avoided.

Both difficulties are easy to solve. If this is noticed during the post-operative course there will be no difficulty in changing the lens to one of proper size. The incision should preferably be made at the same place. If noticed during the operation, the larger lenses can easily be modified before the inclusion. The best way to deal with this incident is to have prepared two lenses with a difference in length of 0.5 mm.

(2) *Miscalculation of the dioptric power of the lens.* This will lead to an imperfect post-operative refraction which can be corrected by changing the lens to one of the right power. To avoid this, the refraction and measurement of the distance of correcting lenses from the corneal surface should be accurate. The maneuvers of substituting a lens are not dangerous.

OPERATIVE COMPLICATIONS

These should not occur if the technique is followed correctly.

(1) *Tearing of the corneal endothelium.* This is produced by the plastic lens if an excessive pressure is exerted in an effort to avoid the pupillary sphincter.

(2) *Dragging of the pupil with the proximal end of the lens.* This should be avoided by sliding the lens gradually up or down the pupil (Fig. 3) centering its position immediately afterwards.

(3) *Loss of vitreous.* This may be due to lack of potentialization, inopportune compression on the eyeball, and imperfect miosis.

(4) *Luxation of the lens by excessive or rough compression.*

POSTOPERATIVE COMPLICATIONS

(1) *Hypertension.*

(a) By neuro-vegetative irritation and blockage of the angle. We have not had any case of this type in our experience.

(b) By blockage of the pupil. This accident is due to a failure of the peripheral iridectomy with persistence of the pigmentary layer or blockade of the iridectomy by one end of the lens. The best prophylaxis is to be sure that the iridectomy has perforated the iris at 12 o'clock and to place the implant horizontally. The pupil is blocked only at the time of operation, before the anterior chamber is re-formed. This occlusion is made more firm when the aqueous is formed and will lead to secondary glaucoma, but this cannot happen if the above technique is followed.

(2) *Pigmentary precipitates or deposits.* In most cases this does not occur. They are very scarce in the majority of cases and disappear in time without any treatment.

(3) *Iritis.* We have never had a case with iritis. We always administer oral hydrocortisone during the first few days after operation.

(4) *Traumatic corneal edema.* This is identical to that which occurs after cataract extraction. It is not frequent and disappears in two or three days.

(5) *Late edema of the cornea.* This follows endothelial dystrophy at the points where the cornea touches the lens. We have yet to see a case.

POST-OPERATIVE COURSE

The complications considered above are exceptional and the post-operative course is very simple. By the seventh day the eye frequently looks as if it has never been touched; it is already quiet and the visual acuity is very good. The first dressing is made on the third day; generally the pupil reacts to light and we instill an atropine solution and use a monocular bandage. On the seventh day the eye is opened and orthoptic exercises can be initiated.

PERSONAL EXPERIENCE

Our first inclusion of acrylic lens in the anterior chamber was in July 1954. In June 1956, 62 patients had been operated on with satisfactory results. Five of these operations were performed after intra-capsular extraction, 29 after extra-capsular extraction (traumatic cataracts or patients under 30 years where total extraction is not indicated), and 28 in non-aphakic eyes (myopia, anisometropia).

VISUAL ACUITY

In all of our cases the visual acuity is better (or at least the same as before operation) with this intraocular lens. In most of the cases the spherical part of the ametropia is totally corrected, leaving the same amount of astigmatism as

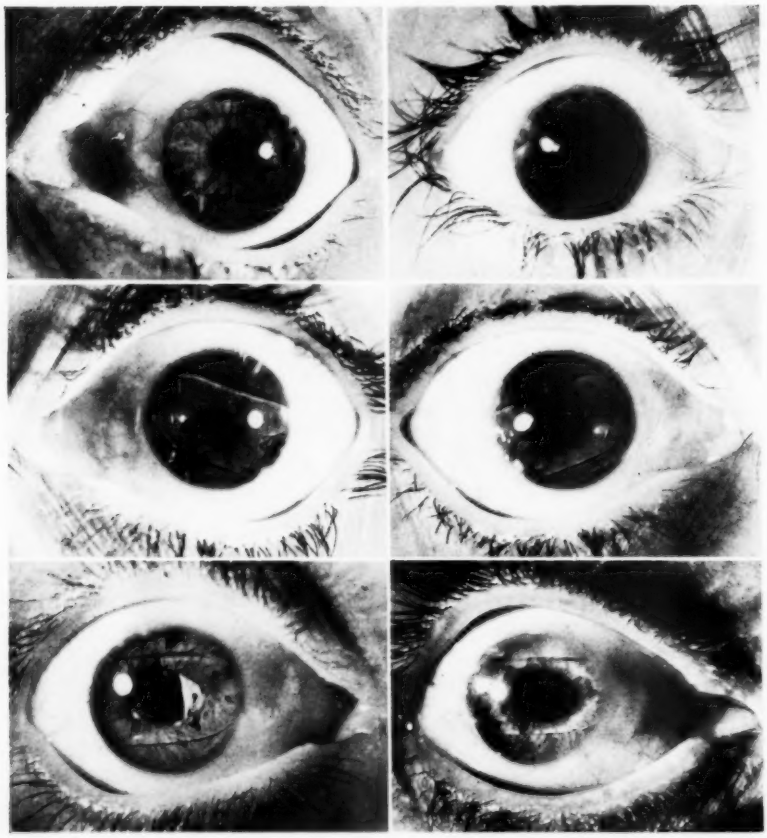

FIGURE 10. *Upper left.* Lens inserted three months after total intracapsular cataract extraction (phakoerisis). Note the small peripheral iridectomy.

FIGURE 11. *Upper right.* Plastic lens placed in a myopic eye where cristalline was "*in situ.*"

FIGURE 12. *Middle left.* Insertion of the lens in a congenital cataract patient who was operated for optical iridectomy and later on extra-capsular cataract extraction, before this lens was placed.

FIGURE 13. *Middle right.* Right eye of the same patient. The lens was successfully placed even in the presence of total iridectomy and prolapse of vitreous in the anterior chamber.

FIGURE 14. *Lower left.* Inclusion in a case with membranous type of cataract. Capsulotomy and an iridotomy at 5 o'clock position to centre the pupil which was deviated towards 9 o'clock were performed after this operation.

FIGURE 15. *Lower right.* Inclusion in an eye operated by intracapsular extraction 3 months before. Note a somewhat deviated pupil because of slightly bigger lens, but it was well tolerated.

before the operation. In amblyopes the re-education with after-images and pleoptics is far better after these inclusions.

BINOCULAR VISION

This is regained spontaneously in the majority of the cases. Systematically we prescribe exercises at the synoptophore to increase the amplitude of fusion. We have seen cases of great myopic anisometropia with suppression develop second degree fusion faculty after this operation.

TONOMETRY

In most of the cases there is a little hypotony (T. Bailliart—10 mm. Hg). After 15 or 20 days the tension tends to normalize.

GONIOSCOPY

If the size of the lens is correct, no modifications of the angle will occur. If the length of the lens is bigger than the diameter of the anterior chamber, a small cyclodialysis is produced (or a depression of the iris root) with secondary pupillary deviation. In no case have we observed any synechiae to the acrylic lens, or in the angle. When the lens is of large size, small zones of partial iris atrophy are observed frequently.

COMPLICATIONS

We have never had any serious complication. Four complications are described which were successfully solved, attaining a good functional result. Those complications were as follows:

In our first case (inclusion after extra-capsular extraction) hypertension by pupillary blockage followed as we had not performed any peripheral iridectomy. With retrociliary diathermic punctures we were able to stop this vicious cycle (blockade—pressure—blockade).

In our third case (inclusion with crystalline lens "*in situ*") the corneal incision was too small. The maneuver of inserting the lens was difficult and a tearing of the corneal endothelium was produced.

During the post-operative period the patient had some photophobia and corneal edema, which necessitated removal of the plastic lens. Lately the operation has been repeated on this patient with favorable results.

In two other non-aphakic cases the iridectomy was blocked by one of the extreme edges of the lens placed vertically. This complication was relieved by performing a new peripheral iridectomy, and in a number of cases in which we suspected this complication, we have avoided it by turning the axis of the lens 90°, i.e., horizontally.

Since then there have been no other types of complications.

Clinical Practice

ACCOMMODATION AND REFRACTION

REFRACTIVE CHANGES IN NORMAL YOUNG MEN

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A.M.A. Arch. Ophth., 1956, *56:* 761–767

The refractive changes that occur in adolescence and early adult life are thought by most physiologists to be associated with the continuing growth process; a few, however, believe them to be due to other causes, such as genetic contributions, racial predisposition, nutritional influences, convergence effects, and the excessive use of the eyes for close work. Except in cases of disease, the problem is ordinarily not of major importance and the changes can easily be corrected by the prescription and use of glasses. The fact that all young men who are physically qualified are now required to spend some time in military service makes it necessary to give more consideration to these refractive changes than they have received in the past. Many adolescents who meet prescribed visual standards at the beginning of their training are not visually qualified at the completion of their course to accept the responsibilities for which they have been trained. Others must be removed from highly technical specialties because their visual acuity has fallen below the required standards. The authorities in charge of training these young men have become acutely aware of the necessity of selecting only those candidates whose vision can be expected to continue to meet required standards after graduation.

For the military ophthalmologist the problem of refractive change in young men has, therefore, become considerably greater than it is for his civilian colleague. Nevertheless, because many candidates consult civilian eye specialists in regard to borderline visual acuity, the subject possesses general interest, and the purpose of this paper is to present observations and conclusions that can be applied to the selection of candidates who must maintain a relatively high visual acuity to continue in certain military categories.

In 1949, the Department of Ophthalmology at the U. S. Naval Academy, Annapolis, Maryland, was asked to determine the reason for the relatively high attrition of midshipmen because of deterioration of visual efficiency, when these same men had been admitted to the Academy as visually qualified. The problem was not a new one and had been previously investigated at the Academy. Corrective measures had been undertaken to improve illumination and diet, as well as to select textbooks with a suitable size of print and reflectance of paper. Firm

adherence to the visual requirements for admission was also demanded. After these factors were brought close to the optimum, a study of the ophthalmic records of four consecutive classes, three of which were then at the Academy, was undertaken.

These records were kept in such a way that at graduation each ophthalmic record had at least five entries and contained sufficient material to permit an over-all evaluation of the four-year ocular history of each individual. This chronologic tabulation shows at what age visual acuity started to diminish and the nature of its subsequent progress through each scholastic year. If the visual acuity fell below 20/100 in either eye, the midshipman was separated from the Academy.

It may be noted that young men at the service academies lead lives so regimented for economy of time that each spends about the same amount of time in classroom and laboratory activities, study, exercise, sleep, and recreation. The diet, carefully planned by dietitians, is the same for all and is generous. At the Naval Academy, the living environment is essentially the same for all the men, and the factors of illumination and light reflectance have been carefully engineered to provide proper study conditions. The level of personal and group hygiene is very high and is so maintained by regulation and by daily inspection. It seems reasonable therefore to assume that the 3700 midshipmen composing this study group led lives so essentially similar that any non-traumatic external factor that might affect the eyes or refractive status of any one would have a similar effect on the eyes of all. Midshipmen are carefully screened physically, psychologically, and academically so that they constitute a highly selected group. Since this is so, their further physiologic development may well be considered the normal biologic expectancy in a controlled environment.

In spite of the propitious influences resulting from careful selection and a controlled environment, the development of some degree of visual impairment was noted in about 18 per cent of the men in each class. The cause of decreased acuity was almost exclusively myopia or some form of myopic astigmatism. The records showed that myopic corrections were prescribed for many men during their first year and that these were rather regularly increased in strength up to the time of graduation. The glasses were prescribed carefully and only when really needed. In reviewing these records, it was noted that most of those needing glasses had shown essentially emmetropic refraction on admission, and that more glasses were issued to younger than to older men.

When the records of two classes—separated according to the age and cycloplegic acceptance of the midshipmen on admission—were studied to determine the incidence of visual defects within the various groups, it was found that 17- and 18-year-old adolescents who have 20/20 vision and whose cycloplegic acceptance is 0.50 D. (or less) of plus spherical equivalent, are apt to present some degree of myopic-type refractive error and diminished visual acuity during the next four years of life. The goal of nature appears to be refractive emmetropia at the end of the period of growth. If that goal is reached before growth has been completed, further development results in the formation of an optical system

that is overly strong in its refractive functions, and some type of myopic defect is produced that prevents clear distant vision. In the present carefully selected group of those who achieve emmetropia early in their adolescence, the tendency to become myopic as physical development continues is striking. As the same pattern unfolds in essentially the same fashion in class after class, it may be taken to represent a normal physiologic evolution, based, apparently, upon a genetically determined predisposition related to the final growth increment, and predictable when evaluated on a mass basis, so that tables of anticipation can easily be constructed to aid in the selection of candidates, or to make it possible to prepare for their eventual disposition.

As adolescence recedes, the relation of age to emmetropic refraction becomes less significant so that at the age of 21 men with 20/20 acuity and an essentially emmetropic refraction have a greater-than-90 per cent likelihood of continued normal vision.

If all adolescent candidates for training in military and civilian specialties in which continued 20/20 acuity is necessary were required to have a cycloplegic acceptance in excess of 0.50 D. of plus spherical equivalent, the attrition from refractive myopia would be less than 10 per cent.

Comment: Refractive changes in eyes, occasioned by growth factors as well as pathologic conditions, have been of interest to ophthalmologists ever since refraction work was first organized as a scientific procedure by Donders. The present study is probably the first, however, in which the conditions of observation have been so rigidly controlled, in that each of the cadets in the Naval Academy is under close observation for four years, with frequent physical examinations, including yearly visual acuity determinations and cycloplegic refraction when indicated. Certainly, in this carefully selected group whose nutrition and living conditions are optimal, refractive changes must be due primarily to growth factors.

The pattern revealed in this study is one familiar to ophthalmologists with long-time experience in refraction. A young child with myopia is a rarity, but myopic individuals are not rare in the general population. Practically all children with apparently normal eyes are hyperopic in early childhood, and, as time goes on, the amount of the hyperopia lessens; many cases remain permanently hyperopic, some practically emmetropic, while others become myopic, apparently quite independently of any use or non-use of the eyes.

In some instances, of course, the process is speeded to such an extent that it becomes apparently pathologic, and in these cases myopia may be found in the pre-adolescent age and often may increase rapidly and consistently beyond the early twenties, the age that usually represents the termination of ocular growth. Such cases may be considered as progressive or malignant myopia and are obviously the result of other than normal growth.

In this paper, the observations and conclusions coincide very well with the experience of most ophthalmologists, and with those observations and conclusions previously published (of which the major contributions are listed in the bibliography).

Clinically, the importance of these observations is two-fold. First, it is helpful to know what will be the probable refractive result of ocular growth in a given child or adolescent; and certainly it suggests that the increment of such growth, in any given year, should not result in a refractive change of more than 0.50 D. to 0.75 D.

When the astigmatic corrections are included with the spherical, it becomes a problem to express the refractive error in simple terms of hyperopia or myopia. The popular

method, and the one adopted in this report, is to utilize the spherical equivalent, which can be described as the actual refractive power in the two meridians located at 45° from the major and minor astigmatic axes. This is of little importance in working with the cadets in the Naval Academy, who have been selected on the basis of a cycloplegic refraction and acceptable visual acuity, but it is of great importance in dealing with the general run of patients, which will include many with high amounts of astigmatism. In the latter cases, there would be no usable correlation between the spherical equivalent and the expected visual acuity. For instance, a patient who, in order to see clearly, requires a lens correction of −1.00 sph. +2.00 cyl. ax. 90°, would have a spherical equivalent of 0.00 D., but, nevertheless, his uncorrected visual acuity would certainly be much less than 20/20. It might be better, for survey purposes among the general population, to utilize the refractive meridian presenting the least hyperopia or the greatest myopia as a basis for a classification.

Another and important factor which must be kept in mind in refraction work is the effect of cycloplegic drugs upon the normal ciliary muscle tone. While the cycloplegic drugs usually used in adolescent and early adult stages do not seem to have the same marked effect in reducing normal ciliary muscle tonus as atropine, they, nevertheless, may relax the muscle tone to some extent and, thus, apparently increase the total hyperopia or decrease the total myopia as compared to the amount usually present. Another source of possible error is found in the mydriasis which results from the use of any cycloplegic drug, inasmuch as the refraction of the eye in the pupillary zone may differ considerably from that in the peripheral area. In the office, and in such surveys as this, these errors may be avoided by adequate post-cycloplegic examinations and by the use of pupillary discs during the cycloplegic refraction procedure.

EDWIN FORBES TAIT

OBSERVATIONS ON THE FOOD HABITS OF MYOPIC CHILDREN

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Miller and Barnet General Hospitals; Guy's Hospital, London, England

Brit. M. J., 1956, *2:* 699–700

An inquiry into the development of myopia in children which included questions about their diet showed that many have rigid likes and dislikes of certain foods leading to a consistent refusal of some items. The main sources of first-class protein are milk, cheese, meat, fish, and eggs. Over a period all the children in a school clinic for refraction were asked whether they consistently refused one or more of these foods. The refusal to take milk as such or as a mainly milk drink was counted as an absolute refusal. A number of children were found to refuse their school milk, thereby providing others with a double or sometimes treble portion.

It was possible to divide the children into groups of myopes who were rapidly

deteriorating, slowly deteriorating, or stationary. A fourth group consisted mainly of hypermetropes with a few emmetropes. Classification of the answers showed that myopes are more fussy about their food than other children. With increasing fussiness there is an increase in the activity of the myopia. The boys with highly active myopia show a refusal rate more than twice that of boys who are not myopic, and the girls a rate over 50 per cent higher. Double refusals are twice as frequent amongst active myopes as amongst others. That girls are more particular about their food than boys is well known, and in all these groups this was confirmed, although the difference is small in stationary and slowly deteriorating myopes. Though the rate of refusal is higher in girls than in boys in each group, it does not equal the rate of refusal for boys in the next group with a higher rate of myopic change.

The percentage refusing a particular source of protein do not provide any conclusive information. The most striking difference was in milk consumption. Over three times as many myopes refused milk as others. It must not be concluded that myopia in children is associated dietetically exclusively with a different pattern of protein consumption, still less with a deficiency in the accepted sense of the word. There is evidence (to be published later) that other food factors are implicated, and in most individual cases the food pattern is in no way basically abnormal even though the myopia may be increasing rapidly. None the less, the positive finding in this investigation is that myopic children are more particular about their sources of first-class protein than other children. This may be connected with their myopia, because girls are more inclined to pick and choose than boys and because the more active the myopia the higher the refusal rate.

THE GLOBE

SIMPLE STUMP FORMATION IN ENUCLEATION AND EVISCERATION OF THE EYEBALL
(Nylon Implantation)

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Ophthalmologica, 1956, *132:* 264–270

For decades the ophthalmologists were engaged in the problem of suitable replacement of the globe in order to obtain better cosmetic results after enucleation and evisceration. Bangerter discusses the features of an ideal implant as follows:

(1) *Ease of Procurement.* Commercial balls are available that no longer make it necessary to use fatty tissue and bone which may be obtained only with great effort.

(2) *Simple Technique of Implanting.* The technique of implanting as a rule, is not difficult, but normal mobility requires the correct attachment of the four rectus muscles. Complicated ball implants, therefore, may require a greater operative skill.

(3) *Short Post-operative Treatment Period.* The ophthalmic practitioner must endeavour to make the after-treatment as simple and as short as possible; therefore, he will avoid a complicated technique.

(4) *Slight Chance of Extrusion.* Prolonged irritation or secondary extrusion is a complication which puts a heavy burden on the ophthalmologic practitioner who treats the patient in the office. Extrusion is a risk associated with commercial implants which are on the market at present.

(5) *Ability to use Usual Type of Prosthesis.* Special prostheses are not yet at the disposal of most of the ophthalmologists and they are very difficult to obtain.

(6) *Good Cosmetic Result.* Complicated techniques with special prostheses give excellent cosmetic results which can not be surpassed. There remains, however, the question of whether practically the same satisfactory mobility of the artificial eye may be obtained with a simpler method, and whether there may be a technique which involves less risk.

The author describes his method for obtaining a simple stump in enucleation and evisceration of the eyeball by implanting a loose nylon ball of his own make. The nylon ball is made up by chain stitches and is inserted in a net which is made up in the same manner. The net is then pulled together, but a thread, 30 cm. in length, is left, so that the implant may be given its final shape before it is implanted into Tenon's capsule. The enucleation is performed according to the usual technique with the aid of local anesthesia using a 2 per cent solution of 1-p-aminobenzoyl-2,2-dimethyl-3-diethylaminopropanol hydrochloride (Lar-

ocaine), epinephrine and a hyaluronidase-Larocaine mixture. After hemostasis has been achieved, the sterilized nylon ball is carried into the well-spread Tenon's capsule. The implant should be of such a size that closure of Tenon's capsule with several fine catgut-sutures can be performed without tension. The average diameter of the implant is 18 mm. Dehiscence must be carefully avoided. The muscles must then be fastened with catgut sutures in such a manner that they are tied not only to Tenon's capsule, but also, in order that the stitches of the nylon-coil are held. In evisceration of the eyeball a somewhat smaller nylon ball is inserted into the scleral cavity. Unsatisfactory mobility of a prosthesis may be the indication for a secondary implantation of a nylon ball after enucleation had been performed previously.

N_1-dimethyl acroyl sulfanilamide (Irgamid) ophthalmic ointment should be applied to the cavity immediately after the operation, a pressure bandage should then be used and ice compresses should be applied on the first day. A prosthesis should not be inserted sooner than three weeks after the operation.

The new method has proved its effectiveness in about 100 patients in whom it has been used in the past several years. Cosmetic results obtained were satisfactory; the usual prostheses could be used; and strabismus was observed only with extreme direction of vision.

The advantages of the method are perfect tolerance of the implant, simple technique of implantation, the possibility of even secondary implantation, short duration of after-treatment, no necessity for special prostheses, and satisfactory mobility.

Comment: The author claims that the implant he advocates fulfills all the features required of a good implant. I have had no experience with the material which he describes. It is known from the studies by Berens and others that nylon sutures are better tolerated than most other types of foreign materials which would tend to substantiate the claims of Bangerter. The results with nylon mesh would seem to be comparable to those with polyethylene sponge reported by Pearlman.

In the last analysis, with all techniques in which a buried implant is used, the result depends on the skill of the artificial eye maker. A good mobile stump is a decided help in securing life-like motion, but it is true that even with the best implant, an unsatisfactory artificial eye can nullify the end result. On the other hand, it is possible for an expert prosthetist to make a reasonably mobile artificial eye even if the motion of the stump is less than satisfactory.

DANIEL SNYDACKER

THE CORNEA

HISTOPATHOLOGY OF KERATOCONUS

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Am. J. Ophth., 1956, *42:* 847–860

Keratoconus or conical cornea has been known to ophthalmologists for many years. Its etiology, however, is still obscure. Since keratoconus in itself rarely leads to enucleation, paucity of pathologic material, even of well-developed keratoconus, is not surprising. Evidently in the past all pathologic material studied represented late stages of the disease after complications. Since corneal transplantation in cases of keratoconus presents such a favorable prognosis, particularly if operated in the relatively early stages, there should be an increasing source of material for histopathologic study in order that the mechanism of the development of the disease may be understood more easily.

MATERIAL AND METHODS

Our material consisted of pathologic disks removed at keratoplasty. A total of 65 such disks collected from the Manhattan Eye, Ear, and Throat Hospital were studied. Each disk was fixed immediately in 10 per cent neutral formol-saline solution, and then embedded in paraffin. The fixed tissue was bisected and sectioned serially in both the transverse and surface planes. In some instances the posterior portion of the disk involved the endothelium. Descemet's membrane and as little as possible of the stroma was mounted.

The essential histopathologic findings in keratoconus (in its early stages) are chiefly confined to the anterior layers of the cornea. It involves the epithelium, the epithelial basement membrane, and Bowman's membrane, as well as the anterior stroma. Changes in the epithelium seem to be secondary since they are found almost exclusively in the presence of changes in the basement membrane and Bowman's membrane, or changes in the endothelium. The degenerative changes in the basement membrane and Bowman's membrane are most likely the initial lesions, because they occur when the other layers of the cornea are normal. It is difficult, if not impossible, to know whether the basement membrane or Bowman's membrane is first involved since their changes are always associated with each other.

Under ordinary light microscopic examination, Bowman's membrane is generally accepted to be a homogeneous, structureless membrane. Examination with the electron microscope, however, shows that it consists of fine fibrils. The first degenerative changes in Bowman's membrane appear to be swelling and

fibrillation. It is quite possible that there is some physicochemical change in its constituents which give it the edematous and swollen appearance and make manifest its fibrillar structure which usually does not show under ordinary microscopy. This fibrillar degeneration extends to the underlying superficial stroma and can be demonstrated more clearly with the phase-contrast microscope. The overlying basement membrane first shows fragmentation, then complete destruction. It does not appear unreasonable to think, therefore, that the cornea becomes weakened by the degeneration of the membranes and superficial stroma, and becomes unable to withstand the normal intraocular pressure. It can not maintain its normal curvature and the result is conical cornea. At this stage, stretching of the cornea, ectasia, takes place without other obvious clinical signs.

It seems likely that the degeneration of the basement membrane and Bowman's membrane, as well as the anterior stroma, plays an important role in the development of keratoconus. As the degeneration develops, its manifestations progress from changes in the staining reactions to multiple areas of loss of Bowman's membrane and most of the superficial stroma. The gaps in the destroyed membrane are then filled with either newly-formed connective tissue that contains focal concentration of keratoblasts, or with downgrowth of epithelium. These lesions appear clinically as linear superficial scars. In addition, we believe that the stretching of the ectatic cornea widens the perforations of Bowman's membrane for the passage of nerves, and that this accounts for the holes in Bowman's membrane found in serial sections.

Folds in the deep stroma and in Descemet's membrane are a common finding in our series. Clinically these are seen as the stromal striae in the deep layers of the cornea. We believe that the deep folds and buckles of Descemet's membrane are emphasized by release of tension after the removal of the disk.

Von der Heydt had observed clinically a very decided change in size and shape of these striae at various times. Schmidt stated that the striae in keratoconus may disappear transiently with a temporary increase in the intraocular pressure, through compression of the globe, abdominal pressure, and so on. It was his opinion that the striae in keratoconus were caused by the contraction force of Descemet's membrane.

In order to exclude the possibility of artefact produced through histologic preparation, we studied a number of disks with other pathologic processes, such as Fuchs' dystrophy and corneal scars due to other causes. They did not show folds in the stroma and Descemet's membrane.

Eight out of 65 cases (12.3 per cent) showed rupture of Descemet's membrane. According to a study by Terry and Chisholm, it appeared that strips of rabbit cornea could be stretched some 10 per cent before they ruptured. Therefore, any overstretching may sufficiently disrupt the continuity of the membranes of the cornea in keratoconus. Hervouet found one out of nine cases with rupture of Descemet's membrane in histologic examination. Clinically Rohrschneider and Stohr reported that it occurred in about 11 per cent of all cases of keratoconus. One would expect higher percentages in specimens that come to pathologic examination, because this would not include the earliest cases.

Since the endothelium is intimately associated with Descemet's membrane, its cells are lengthened and flattened, and the nucleus is reduced to a thin dark particle.

Comment: This study of sixty-five disks from eyes with keratoconus is an important contribution to our knowledge of the pathology of this condition. Although conical cornea can be explained on a genetic basis, the cellular or intra-cellular causes for the weakness of the tissues, leading to gradual thinning under pressure are not yet known.

In this study, advanced cases of keratoconus had changes in all layers. The epithelium in some was reduced to only two cells in thickness and there was an absence of basal cells in some areas. There were multiple dehiscences in the basement membrane. Bowman's membrane was destroyed in some and replaced by connective tissue. The authors also observed destruction of superficial stroma, rupture of Descemet's membrane, and thinning of the endothelium.

A study of early cases of keratoconus revealed the beginnings of the pathological processes in the anterior layers of the cornea, with simultaneous early change in the epithelium, Bowman's membrane, and the anterior stroma. The authors were able to demonstrate a fibrillation in Bowman's membrane and in the anterior stromal fibers which they thought might be the basis for the subsequent pathological changes. They failed to find any histochemical changes in the ground substances.

This report is an important contribution to our knowledge of the histology of conical cornea, and lays the foundation for further research into the etiology.

HUGH L. ORMSBY

THE OCULAR MUSCLES

STEREOPSIS AND DEPTH PERCEPTION AFTER TREATMENT FOR CONVERGENT SQUINT

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The improvement of binocular vision after squint operations, found in patients in whom restoration of binocular vision was not expected, led to a survey of 263 patients—151 without fusion before operation, 112 with fusion before operation—and an additional 20 patients discharged as cured from the orthoptic department without operation. The final value of the stereopsis attained was assessed by depth perception tests and by the cover test, and these findings were also correlated with the amplitude of fusion found on the synoptophore.

The patients studied were chosen from those having had an operation between 1943 and 1953. An effort was made by selecting routine notes at random from the files, and by distributing the cases among different surgeons and years of operations, to form a reasonable sample of the whole. The patients treated by operation numbered 105 males and 168 females, ranging in age from 7 to 30 years. The angle of squint before operation varied from plus 8° to plus 50°; the age at operation was between 5 and 24 years; and the interval between onset and operation varied from 6 months to 19 years. The patients treated without operation numbered 8 males and 12 females, ranging in age from 7 to 21 years.

Depth perception tests were carried out on 69 of the 85 patients found to have postoperative stereopsis, the 20 patients treated without operation, 11 normal subjects aged from 7 to 19 years, and 12 patients without postoperative stereopsis (of whom 7 showed some evidence of fusion). An analysis of the results obtained provides answers to the five questions of major interest in this study. First, what are the factors determining the presence of stereopsis after operation? It is evident that the greater the degree of binocular vision before operation, the greater it is likely to be after operation, and one factor that is known to determine the preoperative binocular vision is the age at onset, as was confirmed by the findings. In addition, it was found that the age at onset is an important factor in determining the presence of stereopsis after operation irrespective of the presence or absence of preoperative fusion. In patients with preoperative fusion, an additional independent factor was the interval between onset and operation. No data were available for the influence of this factor on patients without preoperative fusion. The presence of vertical deviation in patients without preoperative fusion, of a low refractive error in those with

preoperative fusion, and of partial amblyopia in both groups, may have had an adverse effect on the final results, but these factors have little prognostic value.

The second question is: What degree of depth perception is present in patients who show stereopsis on the synoptophore? The striking result is the very poor depth perception attained, both by the postoperative patients and by those discharged as cured without operation. Only 1 of every 10 patients with postoperative stereopsis, and 2 of every 10 discharged as cured without operation, had depth perception approaching normal. Even on the easiest test employed, about 3 patients in 10 showed no evidence of depth perception.

The outstanding factor in relation to the third question—What factors determine the presence of good depth perception in patients with postoperative stereopsis?—appeared to be the interval between onset and operation. In this respect, the results suggest that operation should not be postponed until the presence of fusion can be ascertained. Patients who did not have fusion preoperatively did not do quite so well in the depth perception tests, which detracts slightly from the importance of the development of stereopsis in this group.

In answer to the fourth question—Do clinical tests give a guide to the degree of depth perception present?—it was found that none of the 12 patients who failed to show stereopsis on the synoptophore showed any evidence of depth perception. Of those with stereopsis, the best depth perception was found in patients with a functionally satisfactory cover test, though, even so, only 1 in every 6 of the postoperative patients, and fewer than 2 in every 6 of those discharged as cured without operation, had depth perception approaching normal; in each case about 1 in 6 showed no evidence of depth perception in the easiest test employed. Although there was a good correlation with depth perception, the fusion amplitude did not give any better idea of the depth perception present than that given by the cover test alone.

Finally, the fifth question is—Of what value is their binocular vision to those patients who show stereopsis on the synoptophore but have subnormal depth perception?—The superiority of binocular over uniocular depth perception is known to be most marked at short distances. For a normal observer, binocular vision gives no better depth perception than uniocular vision beyond a distance of about 1,000 m., but at 2 m. its superiority is ten-fold. If an observer, as may well have been the case with many of these patients, had binocular depth perception of one-tenth of normal, or less, it would not be expected to be of much value to him at any distance beyond 2 m. Such patients would make use of their binocular depth perception for close work only, and even so it would be much less valuable to them than to persons with normal vision.

Routine tests for peripheral or paramacular fusion were not carried out on these patients, but experience with such tests suggests that they had peripheral fusion and that this may have been a factor in maintaining the visual axes parallel in patients who were making no appreciable use of binocular depth perception.

Comment: This is a statistical report on 263 patients with convergent strabismus whose degree of binocular vision had been tested preoperatively on the synoptophore. This

examination required a minimal age of five years so that no operation was done under the age of five. The purpose of this report was to note any improvement in binocular vision postoperatively and to analyze factors which influenced the result. In the patients without binocular vision preoperatively, or with mere simultaneous perception, slightly more than 20 per cent developed binocular vision postoperatively. This improvement usually occurred in the first six months of the post-operative period or nearly always within a year of the operation. The presence of simultaneous perception preoperatively increased threefold the chances of attaining binocular vision postoperatively. An age of over two years at onset of the squint, a vertical deviation of less than three prism diopters and a residual angle of deviation of less than five degrees all were favorable. Their opposites all were unfavorable. As the earliest age of operation was five years and the shortest interval between age of onset and age of operation was two years, the effect of early age of operation and short interval between onset and operation could not be analyzed. The findings are in general agreement with current opinion in this country. They are not startling but merely confirmatory.

Of particular interest was the authors' investigation of stereopsis using rod and drop tests. The outstanding finding was that even of those patients showing stereopsis on the synoptophore, only a small percentage had stereopsis approaching normal when the rod and drop tests were used. Thus, they conclude that the chances of attaining useful postoperative stereopsis are very slim.

PHILIP KNAPP

FIRST IMPRESSIONS OF TREATMENT WITH THE EUTHYSCOPE

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Ophthalmologica, 1956, *132:* 322–326

The euthyscope, devised by Cüppers of the Ophthalmological Clinic in Giessen, in an effort to obtain a refined method of macular stimulation, is an ophthalmoscope of strong light intensity, with which a circular illumination of the retina of about 30° can be secured. With the use of lantern slides, a black spot of 5 or 3° can be projected on to the retina in the center of this cone of light. This gives rise to a ring scotoma in which the negative after-image is seen as a dark ring with a white spot in the center. This test is applied to the macula. By means of a system of lenses the black spot is projected as accurately as possible on to the retina with the fovea centralis in the center of the spot. The retina is blinded for about 30 seconds at a very moderate intensity. Cüppers, whose aim was to transform the relative hypofunction of the central retinal part in amblyopia into relative hyperfunction by blinding the surrounding area, noticed that amblyopias which were refractory to other forms of therapy showed rapid and substantial improvement under this treatment. He also observed that

it is often very difficult for the amblyopic eye to present a negative after-image spontaneously. The positive after-image develops, but the negative often fails to appear. He discovered that in these cases the negative after-image can be produced and maintained for a considerable time by rhythmically flickering the light in the examination room at varying degrees of rapidity. In the treatment of amblyopia, use is made of the central negative after-image. While it persists, isolated optotypes are presented, and the patient is encouraged to recognize smaller and smaller ones. According to Cüppers, this method is also useful in the treatment of excentric fixation. Since the patient himself experiences the correct projection or localization of his macula in the form of the after-image, it is possible to turn an excentric fixation into a central one. A few reports have appeared, indicating that treatment with the euthyscope is an enormous step forward.

Since Cüppers believes that particularly long-standing amblyopias can be improved by this device, the author, who has studied it for some time, applied it in a small group of not-too-young children with amblyopia and excentric fixation. His experience in treating amblyopic patients with central fixation has been that the improvement in vision, though far from negligible, was never as much as 0.5 (determined on the letter chart), and he is convinced that no further increase of the visual acuity can be expected in these cases. In the group of children with excentric fixation, of whom four showed fixed excentric fixation, no change in the fixed excentricity was brought about, even with repeated daily training. In a fifth patient, who had deep amblyopia at the start, the usual methods improved the visual acuity to about 0.1. With the euthyscope, a letter chart vision of 0.5 (with errors) has been reached, but the very restless central fixation has shown no signs of improvement.

Experience with these two groups of children has led to the conclusion that treatment with the euthyscope is certainly not a panacea, though it can be used under some circumstances as an adjuvant and a support to other forms of treatment. Furthermore, the method is very time-consuming. In spite of these disappointing results, however, it should be given more extensive tests.

Comment: The author separates excentric fixation into fixed excentric fixation and non-central fixation by the use of the "Visuskop"—an ophthalmoscope manufactured by Oculus which projects a small star onto the retina. The latter type often responds favorably to the usual treatment by occlusion of the non-amblyopic eye, the former does not.

He reports failure in the treatment of four cases of fixed excentric fixation utilizing the method of Cüppers in which the retina surrounding the macula is brightly stimulated in the hope of transforming the relative hypofunction of the macula in amblyopia into relative hyperfunction by blinding the surrounding area.

Although this method of Cüppers is most ingenious, the uniform failure reported by the author is not surprising. The treatment is for such a short time that it would be most surprising if it had worked. Thus, the problem of successfully treating cases with fixed excentric fixation remains an enigma.

PHILIP KNAPP

THE NON-SURGICAL TREATMENT OF COMITANT STRABISMUS

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The rational management of any condition presupposes a knowledge of the causes and of the physiopathology underlying that condition. Although there is much that is obscure about both the cause and the physiopathology of comitant strabismus, it is known that in this condition the visual axes of the eyes are misaligned and that this misalignment is accompanied by well-defined signs and symptoms. Outstanding among these are certain types of refractive errors in definite forms of strabismus, reduced visual acuity in one eye, poor or absent binocular cooperation owing to suppression or anomalous retinal correspondence, and abnormalities in the motility of the eyes.

The extent to which these various signs and symptoms are the cause or the consequence of the strabismus need not be entered into in this discussion, but an awareness of their existence and of the fact that both innervational and noninnervational factors are involved in almost every case of strabismus has a decided practical importance in relation to treatment. Surgical treatment can effect a change only in mechanical conditions: a change in the position of the eyeballs, and a change in the effectiveness of the ocular muscles. Innervational factors are influenced by surgery only indirectly, in so far as a change in the relative position of the eyes may secondarily produce a change in the binocular cooperation. A permanent change in the relative position of the eyes, however, can be obtained only by surgical treatment.

Nonsurgical treatment, on the other hand, can affect the relative position of the eyes only indirectly, by altering the impulses reaching the extraocular muscles. Change so produced is not necessarily permanent. Innervational and mechanical factors are not present in the same proportion in all cases of strabismus. The nature and extent of the factors responsible in each case must be determined, and this is one of the reasons why nonsurgical treatment should always be tried first in every case of squint. Treatment should be started as soon as the strabismus is discovered because, while it is true that not all forms of treatment are appropriate for children of all ages, some form of treatment can be instituted with a beneficial result at any age.

Treatment may be given by glasses, by drugs, by occlusion, by exercises, and by orthoptic procedures. It has long been recognized that the first important step in the diagnosis and treatment of all forms of concomitant strabismus is the determination of the refraction of the patient's eyes and the wearing of an appropriate correction. The method of refraction depends to some extent on the training and preference of the ophthalmologist, but it is generally agreed that in

children under 10 or 12 years of age, refraction in full atropine cycloplegia is indispensable. Opinions differ as to whether one should prescribe the full correction found in atropine cycloplegia, thus correcting for both the latent and the manifest hypermetropia, or make allowance for the cycloplegia. The system found best by the author is based on giving the patient the maximum correction consistent with a reasonable use of the eyes. A reasonable use, however, is a relative concept that differs greatly with the age of the patient. The younger the child, the more likely he is to tolerate a correction which may tend to blur his distant vision. But as he grows older, his horizon enlarges and distance vision becomes increasingly important. By the time he goes to school he should have glasses which insure maximum vision at distance. Only so will he be able to work comfortably and successfully in school. Bifocals are sometimes needed, and prisms may be useful in certain cases, especially after the angle of squint has been reduced by surgical treatment.

In many patients, the effect of glasses is quite obvious from the start. Nevertheless, the accommodation-convergence relationship is not immediately stabilized and at least one or two months should be allowed to elapse before a decision is made in regard to the effect of the glasses on the relative position of the patient's eyes and his binocular cooperation. Special glasses, of course, must be worn much longer before their therapeutic effect can be fully assessed.

Drugs may be used either to make accommodation impossible or to make it unnecessary. In either case, the accommodation-convergence relationship is affected, sometimes with good results, according to those who have used these methods.

Occlusion, which forces the patient to use his amblyopic eye, is an effective remedy for true amblyopia ex anopsia, which is one of the major symptoms in comitant strabismus. In spite of the fact that occlusion is unpleasant for the child and that it may have far-reaching effects on the nervous system, since it entails a transference of dominance to a thoroughly nondominant eye, its beneficial effect on the visual acuity is such that it should be attempted in every case of amblyopia ex anopsia.

The value of treatment by exercises, as opposed to treatment by occlusion, remains to be seen. Orthoptic training, however, is undoubtedly beneficial and it has an important place in the treatment of strabismus. In general, the purpose of orthoptic exercises is to give the patient good fixation and good vision in each eye; to rid him of abnormal suppression and of abnormal retinal correspondence; and to restore fusional movement and with it normal binocular cooperation. Orthoptic training, however, is not always applicable and it should be given only if an orthoptic evaluation of the patient indicates its desirability. In this connection, it must be remembered that nonsurgical treatment cannot be expected to remove permanently an angle of squint of noninnervational origin.

THE LENS

PROBLEM OF BLOOD-LETTING USED FOR PREVENTION OF EXPULSIVE BLEEDING AFTER INTRAOCULAR INTERVENTION

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Expulsive hemorrhage occurred in 5 (0.122 per cent) of 4094 patients operated on for cataract at the ophthalmic clinic of Vienna between 1944 and 1953. The patients were between the ages of 65 and 84 years. In addition to the advanced age, several other concomitant factors such as extensive loss of vitreous, a high degree of myopia, chronic glaucoma and general hypertension were to be considered responsible for the occurrence of the expulsive hemorrhage. Prophylactic venipuncture was performed immediately before the operation as a routine procedure in all patients with a systolic blood pressure of more than 180 mm. Hg. Expulsive hemorrhage, however, occurred in three of the five patients despite venipuncture.

In an attempt to find out whether a drop in blood pressure may be obtained with a blood-letting procedure carried out before the cataract operation, an amount of blood ranging from 300 to 450 cc. was withdrawn from 30 patients with hypertension, 30 to 60 minutes before they were operated on for cataract. The blood pressure was recorded a few minutes before the venipuncture and immediately before the cataract incision was made. Venipuncture did not influence the blood pressure in 19 patients; the blood pressure was increased in 6 and lowered in 5. Only several hours after the operation did the blood pressure drop moderately in all the patients, reaching its lowest level after 36 hours with an average 18 per cent decrease of its initial value. In a second series of 10 patients venipuncture then was performed 16 or 18 hours before the operation. In 8 of the 10 patients the venipuncture did not influence the blood pressure level, while in one it was increased, and in another it was lowered. Lowering of blood pressure occurred also in the 10 patients 24 to 36 hours after the operation with an average 20 per cent decrease of its initial value. The results obtained in these 40 patients were compared with those in 20 hypertensive patients who were operated on for cataract after 24 hours rest in bed and without previous venipuncture. In 13 of the 20 patients the blood pressure was unchanged after 24 hours of bed rest immediately preceding the operation; the blood pressure was increased in 6 patients and decreased in one.

Since both with and without venipuncture the operation for cataract had usually to be performed without lowering of the patient's blood pressure, it is

suggested that venipuncture should be replaced by the administration of a hypotensive ganglionic blocking agent.

Comment: The chief value of this article is the finding that venipuncture prior to cataract surgery does not prevent expulsive choroidal hemorrhage. Fortunately for the patient, this is a very rare complication and no one surgeon has a large series of cases. Such a series could be obtained only in large institutions where a thousand or more cases are operated each year. When one considers that the intraocular pressure is brought to zero at the time of cataract extraction, it is a wonder that the complication is not more commonly seen. The presence of arteriosclerosis and other degenerative diseases would appear to be as important a contributing factor as the systolic pressure. There is no question that patients with severe hypertension are poor surgical risks, and antihypertensive drugs will reduce the chance of hemorrhage whether it be from the iris or choroid.

P. Robb McDonald

THE INTRAOCULAR PRESSURE

GLAUCOMA AND THE SUPERIOR VENA CAVAL OBSTRUCTION SYNDROME

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Ophthalmic literature apparently contains only two reports of cases in which ocular signs and symptoms are described as associated with obstruction of the superior vena cava. The conditions responsible for vena caval obstruction (which are always to be found on the right side of the thorax because of the anatomic position of the superior vena cava), include aortic aneurysms with or without arteriovenous fistula; thoracic neoplasms, either primary or secondary, though chiefly the former; and more rarely such miscellaneous conditions as chronic cicatrizing mediastinitis; enlarged hilar lymph nodes; and intrathoracic goiter.

The venous drainage of the ocular structures, which is of considerable importance in these cases, takes place by way of the vortex veins, the anterior ciliary veins, and the posterior ciliary veins. The vortex veins carry most of the blood from the iris and ciliary body, and the whole of that from the choroid. The venous return from the iris and ciliary body unites with that from the choroid which leaves the eye through the four vortex veins that run obliquely through the sclera in canals 4 or 5 mm. in length. The two superior vortex veins enter the superior orbital vein and the two inferior ones enter the inferior orbital vein. The anterior ciliary veins drain the anterior part of the ciliary muscle and

the posterior ciliary veins drain the posterior portion of the sclera. Eventually, most of the blood from the head is drained by the internal jugular and a relatively small amount from the external jugulars. A small amount returns by way of the sub-occipital plexus into the vertebral and deep cervical veins, from which it passes into the innominate veins.

The symptoms of obstruction of the superior vena cava, which are the result of venous hypertension in the region normally drained by this vessel, vary in severity according to the degree and location of the obstruction and the extent to which collaterals have developed. The most apparent physical signs are the engorged venous pattern and cyanosis in the upper half of the body. In acute obstructions, marked edema of the face and neck may occur, but edema is less striking in the slowly progressive, more chronic obstructions in which there has been time for the development of extensive collateral circulation. All of the symptoms are intensified with recumbency. Many patients have dyspnea, orthopnea, and periodic bouts of hyperventilation—believed by some to be due to an increased intracranial pressure with tissue stasis of the brain. The increased intracranial pressure may give rise to headache, stupor, somnolence, vertigo, mental changes, and convulsions.

In the first of the patients reported on in the literature, the ocular pressure, which measured 18 to 20 mm. Hg (Schiøtz) in each eye, rose to 35 mm. Hg in each eye when the patient changed to a recumbent position. The second patient had a pressure of 35 mm. Hg in the right eye and 42 mm. Hg (Schiøtz) in the left eye; in this case, the pressure could be controlled by the use of pilocarpine drops.

Six additional patients with obstruction of the superior vena cava in whom ocular signs and symptoms were present have now been studied. The ocular signs found in these patients include edema of the lids and conjunctiva; prominence of the periorbital, conjunctival, and episcleral veins; and a prominence of the globes or slight degree of exophthalmos, nonpulsating in nature. The pupillary reactions and ocular muscle balance are usually normal. The fundi generally show some evidence of venous engorgement and may show some blurring of the disk margins. The ocular tension in the upright or semi-reclining position may be either normal or elevated, but it always rises when the patient is placed in a recumbent position. The signs are more pronounced on the right side and are all aggravated by a change to the reclining position. The tension may be reduced by the instillation of pilocarpine drops. All of these signs appear to be the direct result of obstruction of the superior vena cava by a mediastinal mass that interferes with the venous drainage from the eye and orbit. The glaucoma in these patients must likewise be considered secondary in nature, that is, secondary to the venous obstruction. In each of these 6 patients, the assumption of a recumbent position was followed by a rise in the intraocular pressure of from 7.7 mm. Hg to 27.2 mm. Hg. In the venous congestion test for glaucoma, a rise of more than 6 mm. Hg (Schøtz) after congestion has been maintained for one hour is considered pathologic. In the cases reported here the rise in intraocular pressure occurred almost immediately after the patient had been placed in a horizontal position.

The response of the intraocular pressure to the local instillation of pilocarpine in these patients has been examined to see whether it throws any further light on the antiglaucomatous effects of pilocarpine, which are at present the subject of many differences of opinion. If it can be assumed, as seems likely, that the increased venous pressure in cases of glaucoma associated with obstruction of the superior vena cava, has a damming effect as far back as the intrascleral venous plexus and increases the resistance to aqueous outflow, it would not be unreasonable to suppose that pilocarpine reduces the pressure in the episcleral vessels. This reduction of venous pressure in the episcleral veins would be followed almost immediately by a fall in pressure in the intrascleral venous plexus. This, in turn, would result in a diminished resistance to the outflow of the aqueous, and the accompanying increase in the coefficient of facility of outflow would lead to a fall in the intraocular pressure. In the two cases in this series in which there was no appreciable drop in the intraocular pressure, it may be assumed that, although the pilocarpine had reduced the pressure in the episcleral veins, the reduction was not sufficient to decrease the resistance to aqueous outflow, and hence the intraocular pressure remained constant.

It may be noted that there was no pathologic cupping of the disks in these patients, and that the central visual fields were normal.

Comment: The intraocular pressure elevation produced by obstruction of the superior vena cava fits in well with other secondary glaucomas due to interference with venous drainage. Among these are total ligation or obstruction of the vortex veins or of the anterior ciliary veins, and the secondary glaucoma associated with pulsating exophthalmos due to arteriovenous aneurysm in the cavernous sinus. In the latter, the tension usually has not been high (not over 35 mm. Schiøtz 1924 scale, in the cases observed by this editor), and like the cases described in this article, are not symptomatic.

Two important aspects of this type of secondary glaucoma are the elevation of pressure in the recumbent position and the lowering of pressure in some cases with pilocarpine. The elevation of pressure in the recumbent position is an exaggeration of the normal slight variation in intraocular pressure when comparing the sitting and recumbent positions. Goldmann's normal intraocular pressure reading of 15.5 mm. as measured with the applanation tonometer in the sitting position is evidently equivalent to 16.5 or 17 mm. when measured in the recumbent position. The effect of the change in position is the basis of the Schoenberg provocative test for glaucoma.

The lowering of pressure with pilocarpine makes it difficult to understand the mode of action of pilocarpine. Since the angle is normal and only the external venous pressure is elevated, it is difficult to explain the lowering of pressure by reduction of the pressure in the episcleral veins as the suthor suggests. It is probably true that our present explanations of the effect of pilocarpine are inadequate.

H. Saul Sugar

THE ANATOMY OF THE TRABECULAR MESHWORK AS SEEN IN TANGENTIAL SECTION

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A clear understanding of the anatomy of the trabecular meshwork can not be obtained from the study of meridional sections, because they provide only an unsatisfactory lateral view of this structure. Histologic studies of tangential sections, made by various authors at the turn of the century, yielded much valuable information, although the technique used in preparing the specimens was crude. The preparations were made by immersing the eye in water and teasing the meshwork loose with dissecting needles. The entire meshwork was then examined on a slice. This crude technique seemed to the present author to be a source of possible error and distortion and he therefore studied the trabecular meshwork of 16 apparently normal eye-bank eyes, 8 eyes enucleated because of enoplastic disease, and 12 eyes with early open angle glaucoma, using serial tangential sections made *in situ*. This report deals only with the data obtained from eyes with normal angles; the trabeculae of the glaucomatous eyes are still studied and will be reported on later.

The eyes were obtained from the Stanford Eye Bank and from unused callottes of the Stanford Eye Pathology Laboratory and the Armed Forces Institute of Pathology. More than 700 microscopic slides of the meshwork have been examined. Experiments showed that with gentle pressure the equatorial curve could be partially flattened, with no distortion of the anatomy and yet with much more of the meshwork present on a single slide than when the original curve was retained. By this method, a section of wet tissue 2 to 3 mm. on each side of the limbus and 10 to 20 mm. in length is cut parallel to the limbus. This strip of tissue, which, of course, has the meshwork along its entire length, is placed in melted paraffin with the inner surface down. It is then gently compressed from above with a flat instrument. The bottom of the pan is cooled rapidly with ice, and the compressing weight is removed. Serial sections are then made from within, outwards. Alternate slides were stained with Masson's trichrome stain. A variety of stains, including hematoxylin and eosin, periodic acid-Schiff, and Verhoeff's elastic stain, were used on the remaining slides.

Viewed tangentially, the trabecular meshwork is seen to be strikingly more complex than when it is seen meridionally. Controversy over what is uveal meshwork and what is corneoscleral is easily resolved, for these structures are seen in tangential section to have quite distinct anatomical features. Traced in serial sections from the anterior chamber outwards to Schlemm's canal, three areas with distinctly different histologic characteristics can be seen: (1) the uveal meshwork (the inner lamellae); (2) the corneoscleral meshwork (the middle and largest portion); and (3) the inner wall of Schlemm's canal, the "pore tissue."

In all of the eyes studied the uveal meshwork was always present; indeed, its appearance was so striking and so characteristic that it served as a landmark in locating the meshwork on the slide. It consists of the inner one or two lamellae. A lamella consists of a meshwork of small beams lying in a single plane. Each beam is circular in cross section and is made up of a central core of collagen fibers covered by an endothelium containing cells with flattened nuclei. The average diameter of a uveal beam is 4 μ. The beams are arranged to form large irregular spaces often trapezoidal or rhomboidal in form. These openings are irregular and have no definite orientation. They vary in size from 25 μ to 75 μ across. The large elliptical nuclei with prominent nucleoli, which have been described as endothelial cells, lie outside the collagen core which makes up the bulk of the beams. These nuclei closely resemble the fixed cells of the sclera and the cornea. A barely visible transparent tissue, as seen with Masson's stain, covers the collagen beams. Each uveal lamella is attached on one side to the tissue at the end of Descemet's membrane (Schwalbe's line) and on the other to the ciliary muscle, principally to the longitudinal fibers. Occasionally a uveal lamella courses posteriorly to attach to the iris, to form an iris process. In every case in which there was a connection between the trabecular area and the iris, the tissue was that of uveal meshwork and not iris.

The beams of the corneoscleral lamellae are broad and flat, measuring from 3 $\mu \times 7$ μ to 3 $\mu \times 20$ μ in cross section. Each beam is composed of a number of collagen fibers running in an equatorial direction. Numerous elliptical openings may be seen, with their long axes parallel to the direction of the fibers. From the orientation of these openings it would seem that contraction of the ciliary muscle would make them rounder and therefore larger. This point is now being investigated. The lamellae are attached on one side to Schwalbe's line and the deep corneal stroma and on the other side chiefly to the scleral spur, although the deepest ones may sometimes be attached directly to the meridional fibers of the ciliary muscle. Interlamellar beams may be seen, but are uncommon. Endothelial cells are attached to the surface of the collagen beams, just as in the case of the uveal meshwork. Because nuclei are present on both surfaces of each beam, the number of lamellae may seem to be greater in meridional section than it actually is. Usually, there are from 8 to 14, set farther apart near the ciliary body and the scleral spur than in the neighborhood of Schwalbe's line, where they appear densely packed and are hard to count in meridional section. The appearance of the corneoscleral trabeculae varies greatly with age. In children and young persons the collagen component is much less and the endothelium is more prominent. Indeed, the endothelium may even obscure some of the openings so that the typical elliptical openings, though present, are harder to find in the young. In older persons the increase in the collagen makes the anatomy of the openings in the meshwork easier to see.

When the size of the openings in the uveal and corneoscleral meshworks is traced in serial tangential sections from the anterior chamber to Schlemm's canal, it can be seen that until the region of the inner wall of Schlemm's canal (the "pore tissue") is reached, the openings are much larger than the 1 μ to 2 μ size demonstrated by other workers. The small-sized openings or pores must

therefore be in the region of the inner wall of Schlemm's canal. The tissue between the innermost corneoscleral lamellae and Schlemm's canal is difficult to study in tangential section. The inner wall of the canal is very irregular, having frequent, sometimes angular, outpouchings into the lumen of the canal. The thickness of the pore tissue varies greatly in different persons and even in different areas in the same person. It is usually thinner in the young, and in some older persons it may become as much as 10 times its usual thickness of from 5 μ to 7 μ in certain areas.

The endothelial-lined inner canals described by Sondermann (1930) can not be seen in tangential sections and therefore may be regarded as artefacts. The nature of the direct openings in Schlemm's canal is still a matter for speculation and investigation, but it may be that the endothelium surrounding a single collagen fiber is in contact with the endothelium surrounding the adjacent fibers, with no spaces being present as they are in the meshwork itself. The fluid, under pressure, would then pass through by slightly indenting and squeezing between the endothelial membranes. Openings of the small size of from 1 μ to 2 μ could be better explained in this way than by supposing the existence of an endothelium-lined canal, which would have to have a lumen less than one-fourth the size of a capillary.

Comment: Today's interest in the possible part the corneoscleral trabeculum plays as the site of resistance to outflow of aqueous in adult primary glaucoma has led to a timely acceleration of interest in the details of the trabecular anatomy. The divergence of opinion as to what the uveal meshwork consists of, (Burian, 3 portions; Ashton, 2; and Flocks, 1) can not be settled yet. However, Flocks' finding that the iris processes consists of uveal meshwork and not iris tissue is of interest to gonioscopists.

There is excellent correlation between Ashton's and Flocks' anatomic findings as far as the lamellae are concerned. Both believe that the "internal canals" are artefacts but that tortuous, open, narrow communications do exist between the anterior chamber and Schlemm's canal.

It is to be expected that the actual nature of the pore tissue will be determined more by staining and by chemical than by histologic studies in the near future.

H. Saul Sugar

TONOGRAPHY IN THE CLINICAL MANAGEMENT OF GLAUCOMA

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A.M.A. Arch. Ophth., 1956, *56:* 797–818

The conclusions presented in this paper are based on 600 tonographic studies on 239 eyes with various types of glaucoma. The method used was the one described by Grant, which has proved invaluable in the investigation of certain phases of glaucoma, especially in relation to the flow of aqueous into and from the globe. Much of his work in glaucomatous eyes was repeated in these studies, and the results have confirmed his findings, which strongly support the gonioscopic classification and concepts of primary glaucoma. They indicate that the underlying cause of acute congestive glaucoma is a narrow angle. Except for the narrowness of the angle, the eye is normal and behaves in a normal manner. The flow of aqueous from the eye is normal during periods of normal tension. Acute congestive attacks result from closure of the angle by the root of the iris, a concept supported by the finding of a marked diminution of aqueous outflow by tonography. In narrow-angle glaucoma, during phases of normal tension, either before a mydriasis test or after the termination of an acute attack, aqueous outflow is within normal limits, but during an acute congestive attack, when the angle is assumed to be closed, it is greatly diminished. In chronic congestive glaucoma, after partial or complete angle closure has resulted from synechia formation, the reduction in aqueous outflow is in proportion to the level of ocular tension, or, in other words, to the extent of synechia formation.

Tonography in chronic simple (wide angle) glaucoma indicates an obstruction somewhere in the corneo-scleral wall, in the canal of Schlemm, or in the channels which carry aqueous away from the trabecular and canal of Schlemm mechanisms. The obstruction is usually in proportion to the severity of the glaucoma. When the disease is mild and the tension low, the aqueous outflow may be within normal tonographic limits, but when the disease is severe and the tension high, the outflow is usually definitely reduced.

Indications are that the water provocative test is a more reliable aid in the diagnosis of chronic simple (wide angle) glaucoma than tonography, especially if importance is attached to rises in ocular tension of 6 mm. Hg or more. The diagnosis, however, must be made on the picture as a whole, because no single diagnostic feature is infallible. Any patient showing a coefficient of aqueous outflow of 0.15 cu. mm./min./mm. Hg pressure or less on tonographic examination should be kept under observation. Aqueous outflow values of 0.11 cu. mm./min./mm. Hg pressure or less are probably indicative of glaucoma, because such values have not been found in normal eyes.

A study of 80 eyes not treated with miotics showed them to have an average

coefficient of outflow of 0.11 cu. mm./min./mm. Hg pressure; in the same eyes under miotic therapy, this value rose to 0.18 cu. mm./min./mm. Hg pressure. There was no particular relation to ocular tension. The K value, or net rate of aqueous outflow, was unchanged. Although the increase in aqueous outflow was never so dramatic as that which occurred after an acute attack of glaucoma had been brought to an end by miotic therapy, these findings seem to be significant, apparently indicating that miotics act through the mechanism of increased aqueous outflow.

A special effort was made to assess the effect of medical therapy. The data obtained indicate that, in general, eyes that lose visual field on miotic therapy have a lower aqueous outflow than eyes that retain their field. However, impaired aqueous outflow during miotic therapy for wide-angle glaucoma does not indicate that visual field loss will occur, nor does it serve as an indication for surgical treatment for any given eye. Progressive loss of visual field or an ocular tension uncontrolled on miotic therapy remains a better indication for surgical treatment in chronic simple glaucoma than a failure of miotics to bring about a normal coefficient of aqueous outflow.

The average coefficient of outflow in 16 aphakic eyes was found to be 0.09 cu. mm./min./mm. Hg pressure. This figure seems to be significant and to indicate that the disease is obstructive in origin. This was also true of juvenile glaucoma, in which the average coefficient of outflow in 16 eyes was 0.08 cu. mm./min./mm. Hg pressure.

The greatest clinical value of tonography rests in the evaluation of narrow-angle glaucoma and in its use as an adjunct in the diagnosis of chronic simple glaucoma.

Comment: The authors consider the term pre-glaucoma to be an excellent term and refer to Gradle's paper on the subject. They state that Gradle used the term to designate those eyes with very narrow angles where the ocular tension could be made to rise with pupillary dilatation. In the paper referred to, Gradle considered two forms of pre-glau-glaucoma, one in the "acute, shallow-angle type," the second the "chronic, deep-angle form." Therefore, strictly speaking we should refer specifically to angle-closure glaucoma and either define the term more narrowly or use such a term as pre-acute-glaucoma.

One can not overemphasize the statement that there is a range of error of ± 0.04 in the coefficient of outflow. Because we are most interested diagnostically in tonography in borderline cases, not only are we faced here with an equivocal zone between 0.11 and 0.20, but the additional error makes the diagnostic problem even more difficult.

In regard to the question of the comparison of the water test and tonography, the use of a 6-mm. rise as the criterion of a positive water test, introduces here again a zone of uncertainty since a significant per cent of normal patients will show such a rise. It would appear that one should not consider which is the better test but use the two as adjuncts to each other. The water test, simpler, should be used first and if negative, tonography then done. The authors are wise in advising that diagnosis be made on the over-all picture since no single diagnostic feature is infallible.

This commenting editor cannot help but feel that, since the introduction of tonography, many clinicians, unjustifiably, have lost confidence in their ability to diagnose and treat the glaucomas. They read the reports of studies on angle-closure glaucoma with tonography

and fail to realize that these studies are actually corroborating what we have known clinically for some time—that in the interval or pre-acute phase of this form of glaucoma, the aqueous circulation is normal, and that when the trabecular spaces are closed off by the apposition of the iris root the outflow naturally is markedly depressed. When the tension is elevated in such a case and when the angle is gonioscopically closed we gain no information from tonography. It can be of help in borderline cases, however, when the tension is normal after repeated mild attacks, and one desires to know whether enough of the trabecular spaces have been blocked to interfere with the success of peripheral iridectomy.

The conslusions of the authors appear to be very reasonable in their evaluation of the usefulness of tonography in its practical clinical application to glaucoma.

H. Saul Sugar

NEUROLOGY

OPTICAL LESIONS IN THE COURSE OF TUBERCULOUS MENINGITIS (PATHOGENIC AND THERAPEUTIC CONSIDERATIONS)

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Bull. Soc. opht. France, 1956, *35:* 509–520

The optical lesions of tuberculous meningitis and their ophthalmoscopic manifestations are so frequent, so important as regards visual function, and so useful in early diagnosis that they deserve careful consideration, both in relation to their symptomatic significance and to their pathogenic interpretation. Papillary edema, which is the most frequent ocular manifestation of the disease, is usually bilateral, sometimes differing in degree in the two eyes, and may appear either early or at a somewhat later stage. The changes in the fundus may consist of simple vascular congestion; a hyperemic optic papilla with a blurred outline; more or less intense papillary edema that may even amount to genuine papillary stasis, less pronounced, however, than that accompanying endocranial tumors; papillary pallor; or optic atrophy or subatrophy. When miliary tubercles are also present in the choroid, as sometimes happens in patients with tuberculous meningitis and miliary tuberculosis, the diagnosis can be made without hesitation.

Data obtained since 1946 (when streptomycin therapy, by prolonging or saving the lives of patients with tuberculous meningitis, made it possible to follow the course of the ocular lesions) seem to show that in most cases true optic neuritis is not present and that the papilledema is due chiefly to mechanical

causes, especially the disturbed circulation of the optic nerve and its sheaths. Occasionally, however, papilledema (usually unilateral) may follow a local reaction caused by inflammation of the choroid accompanying the presence of tubercles. Edema of this type, which disappears with cicatrization of the tubercles, must be clearly distinguished from the bilateral papilledema caused by the basilar meningeal disease.

Circulatory disturbances also are largely responsible for simple papillary hyperemia and pallor, which may have a transient effect on the nerve fibers and the transmission of visual stimuli. Optic nerve atrophy and subatrophy, on the other hand, are accompanied by more or less severe changes in visual function and especially in the visual field; in many cases, a process of opto-chiasmatic arachnoiditis is present. As the meningeal condition clears, a new clinical picture, that of the serofibrinous arachnoid, appears, and this presents the most important problem to be met to-day, so far as the preservation of sight is concerned.

The most recent therapeutic advance in the treatment of tuberculous meningitis is the use of cortisone, which should be given early in connection with antibiotics and preferably by the intracranial route. Whether the administration of cortisone will tend to prevent the appearance of optic nerve lesions and especially optochiasmatic arachnoiditis is not yet definitely known. Nevertheless, comparison of the results obtained in 30 patients treated by the usual method without cortisone and those obtained in 20 others treated during the last year with the addition of cortisone by the intracranial route, indicates that the treatment of choice, both for the prevention and for the cure of ocular complications in tuberculous meningitis is the prompt administration of cortisone. Antibiotics should be given by the suboccipital route, rather than the general one, since this is the only method that assures a sufficient concentration in the basal cisterns and the vaginal spaces of the optic nerve.

Comment: The occurrence of optic atrophy in tuberculous meningitis is a recent phenomenon, based on the higher cure rate with the various antibiotic combinations useful in tuberculosis. The survey of cases in Baltimore, by Dr. Frank Walsh, which was reported in the Academy Symposium on Diseases of the Optic Nerve in 1955 indicated an incidence of six cases of bilateral optic atrophy in 108 proved tuberculous meningitis patients. They evidently were due to direct optic nerve damage, although prior observations of edema of the disks were not given. Whether the late changes described by Dr. Alajmo are truly due to an opto-chiasmatic arachnoiditis, or to direct involvement of the optic nerves themselves would be difficult to estimate except by surgical or autopsy exploration, and I assume that the patients cited as good results did not reach the necropsy table. Opto-chiasmatic arachnoiditis accepted as a disease entity without such proof is more popular in the French literature than in our own.

The use of cortisone in such a patient intracranially with active tuberculous infection present is somewhat horrifying to one accustomed to searching for active tuberculosis in any patient to whom systemic steroids are to be given. The merits of this method will certainly require confirmation before whole-hearted acceptance is warranted.

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OCULAR CONSIDERATIONS IN FACIAL PARALYSIS

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Facial paralysis, by involvement of the orbicularis oculi, may cause serious complications in the eye. In addition to the therapeutic problems presented by the ocular complications, facial paralysis presents a diagnostic problem in the localization of the facial nerve lesion. When it occurs in conjunction with various ocular palsies, it is a sign of considerable localizing value.

The ocular complications of facial paralysis consist of epiphora, paralytic ectropion, and lagophthalmos. Epiphora is often the first and in mild cases the only symptom of paralysis. It is always present and is due both to the falling away of the lower lid from the globe with eversion of the punctum, and to the loss of pumping action of the lateral portion of the orbicularis muscle. Paralytic ectropion, which may follow longstanding paralysis in younger persons but usually appears early in older ones, exposes the conjunctiva to the changes common to all types of ectropion. Lagophthalmos, or inability to close the lids, may result in serious damage to the cornea from exposure and desiccation. Corneal ulceration with all its disastrous sequelae may occur.

A diagnosis of facial paralysis may be made on a history of epiphora, inability to close the eye, difficulty in articulation, and a sensation of stiffness in the affected side of the face. As an adjunct to clinical diagnosis, the study of the electrical reactions of the facial muscles may be helpful. An intact nerve contracts with either faradic or galvanic stimulation, indicating that the nerve is capable of conducting an impulse. When the nerve has degenerated and the muscle is still intact, a contraction takes place with galvanic stimulation only. When no contraction takes place with either current, the muscle fibers have undergone the "reaction of degeneration."

Facial paralysis may result from lesions which are supranuclear, nuclear, or infranuclear. In a supranuclear lesion, the muscles of the upper face are only slightly affected, while in nuclear and infranuclear lesions the upper and lower facial muscles are equally affected. Supranuclear lesions may be divided into cortical lesions, which produce the dissociated facial weakness known as mimic paralysis, characterized by loss of emotional movements with retention of voluntary ones; internal capsule lesions, in which the muscles of the upper face are only slightly affected and emotional movements are unimpaired, but voluntary movements of the lower face are paralyzed; and interpeduncular space lesions, which lead to contralateral hemiplegia and facial paralysis, with homolateral third nerve palsy (Weber's syndrome). The excitability of the facial nerve to faradic stimulation is not diminished in supranuclear lesions, and the reaction of degeneration does not take place in the facial muscles.

The nuclear and infranuclear lesions, which may be considered together, are

(1) pontine lesions, characterized by involvement of the adjacent structures; (2) cerebellopontine angle lesions, the commonest of which is an acoustic neuroma; (3) petrous temporal bone lesions, in which the facial nerve may be damaged by fractures, middle ear infections, surgical operations on the ear, and congenital lesions; and (4) lesions in the stylomastoid foramen, in which the facial nerve is subjected to some form of acute inflammation that produces the familiar clinical picture of Bell's palsy.

The ocular management of facial paralysis depends on the degree of paralysis, its anticipated duration, and the associated neurologic lesions. The aim of treatment is to prevent complications affecting the cornea and lids, and the principal problem is to decide which cases require tarsorrhaphy. For purposes of discussion, the cases may be divided into four groups: Group 1 consists of supranuclear lesions in which the orbicularis is only slightly affected so that no treatment is needed; group 2 consists of lower motor neuron lesions in which recovery may be expected in a matter of weeks; group 3 consists of lower motor neuron lesions in which recovery is delayed for months or years; and group 4 consists of lower motor neuron lesions with an associated trigeminal lesion, in which there is loss of corneal sensation accompaning the facial paralysis. Patients with group 2 lesions require instruction (a) in the proper technique of blotting the tears, rather than wiping the eye, which helps to prevent eversion of the punctum and paralytic ectropion; (b) in moistening the cornea by "digital blinking," that is, looking down and drawing the upper lid over the eye with a finger; and (c) in the use of a bland ointment at night. In the absence of paralytic ectropion, patients with group 3 lesions may follow a regimen similar to that for group 2 lesions, the cornea being carefully watched for possible abrasions. As an added protection, a Tovell shield may be prescribed, but if these measures fail to protect the cornea sufficiently, a tarsorrhaphy is indicated and should be carried out promptly. Prompt tarsorrhaphy is also indicated when paralytic ectropion develops, as it usually does in older patients. Patients with group 3 lesions and those with group 2 lesions in which the paralysis has lasted longer than expected should be given electrical stimulation to the facial muscles to prevent their undergoing the reaction of degeneration.

Tarsorrhaphy is mandatory for patients with group 4 lesions and it must be instituted early, because the eye is in grave danger from both lagophthalmos and neuropathic keratitis.

Comment: The problem of protection of the cornea in lagophthalmos is an ever-present one. The author has presented a most lucid account of facial nerve lesions and indicated therapy. In the lesion which may be expected to be transient there must be frequent observation of the eyes, including the use of fluorescein for possible early punctate staining. This is more frequent as an early sign than the abrasions mentioned in the article. The relatives or parents should be instructed to watch for exposure of the cornea during sleep. If this is marked, the eye should be bandaged shut during the night with an eye pad liberally coated with vaseline. For routine protection during the day we prefer the instillation of 1 per cent methylcellulose drops at regular intervals. If there is any question of delay in recovery, or if superficial staining persists, a lateral tarsorrhaphy should be performed. I would certainly agree that any patient with evidence of both trigeminal and

facial nerve involvement should have immediate tarsorrhaphy, usually a two-band procedure with a central aperture for vision. This should not be divided before 6 months, and preferably the nasal band is to be severed first, with a period of observation before opening the second band. In addition to the causes mentioned by the author, occasionally this state will appear after trigeminal rhizotomy, although less frequently since the use of decompression of the trigeminal root rather than sectioning it.

A further most important group of patients should be mentioned—those in coma for various causes. In such a patient the exposed corneas may be overlooked in the concern for the more proximate disease process, or the general prognosis may seem so poor that the eyes are ignored. An occasional patient will recover unexpectedly, only to suffer the corneal scars sustained through exposure. In such patients the eyes may be padded with well-lubricated pads, methylcellulose may be instilled as necessary, or preferably a Frost suture should be used to close the eyes temporarily. This can be done safely and quickly at the patient's bedside.

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THE PUPIL

THE PUPILLARY CHANGES IN THE HOLMES-ADIE SYNDROME

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Since the appearance of Adie's original observations (1931, 1932), a considerable number of publications have dealt with the description of cases in which widely varying pupillary disturbances were associated with abnormalities of tendon reflexes and in which syphilis could be ruled out as a causative factor.

The author states as his purpose "to unify the many pupillary variants and to understand how the disturbance develops." Fourteen cases were presented. Syphilis was ruled out in all of them. In 13 cases all or some of the tendon reflexes were sluggish or absent. Irregularity of the pupillary shape was a constant finding and, in contrast to Adie's and most other authors' descriptions, the abnormal pupil was not always found to be large. Nine cases had pupils of less than 4 mm. in diameter, one as small as 2.5 mm. While Adie and most other authors stated that about 80 per cent of the patients show the pupillary involvement on one side only, 8 of 14 cases described had bilateral pupillary changes. The accommodation was found to be slow or tonic in 9 cases.

In the "complete" form of Adie's syndrome, the pupil is "tonic." It reacts poorly, if at all, to light, but a slow and delayed pupillary contraction appears

when the patient makes an effort at fixing on a near point. This movement may be very extensive and may even exceed the normal pupil's response. When the near vision effort is relaxed the pupil fails to re-dilate promptly and may remain smaller than the normal pupil for some time.

The causative condition for this pupillary syndrome has been thought to be located in the "vegetative portion of the third nerve nucleus" (Behr, Adie), the ciliary ganglion (Scheie, McKinney and Frocht), or in supranuclear centers, leading to sympathetic irritation (Garcin and Kipfer, Lowenstein and Freidman). Sympathetic insufficiency has been assumed by Alajouanine and Morax and by Graveson.

The question of sympathetic involvement was studied by infiltrating the stellate ganglion with 5 cc. of a 1 per cent procaine solution. It was reasoned that if sympathetic irritation was in some way responsible for the tonic pupillary response, interruption of the sympathetic path should nullify the sympathetic effect and eliminate the tonicity; if, on the other hand, a sympathetic lesion was involved, the procaine block could not further affect the pupil. It was found that the effect of the injections varied among patients. In some cases, the pupil hardly contracted; in others, it contracted extensively. The reactions to near and distant vision were not altered in speed, although their extent was often reduced by the smaller initial size of the pupil. It was concluded that neither sympathetic irritation nor sympathetic damage was responsible for the pupillary tonicity. This opinion was further strengthened by the observations that the Adie pupils dilated normally to conjunctival instillation of cocaine (2 drops, 3 per cent) and homatropine hydrobromide (2 drops, 0.5 per cent), and failed to respond to adrenalin (0.1 per cent).

Some of the cases showed hypersensitivity to cholinergic drugs. Thus, in a few instances, the iris reacted excessively to physostigmine sulphate (0.25 per cent), and in 14 of 19 eyes examined, mecholyl caused pupillary construction.

The author agrees with Scheie (1940) that the tonicity is probably the expression of hypersensitivity to acetylcholine which develops after parasympathetic denervation. The sensitivity to cholinergic drugs was found greatest in pupils with the most striking "tonic" contraction to near vision, i.e., incomplete parasympathetic denervation. Conversely, when the parasympathetic damage was acute or extensive, no hypersensitivity was found. In one case, a large, fixed pupil was found to be "tonic" and hypersensitive one year later. "The lesion is in the efferent parasympathetic pathway, and is probably postganglionic. Depending on the respective degree of paralysis and supersensitization, wide clinical variations may be met, but two broad types are recognized—'paralytic' and 'tonic.' The natural history of the disease may be one of repeated episodes affecting the pupils, the function of accommodation and the tendon reflexes in turn."

Comment: The paper gives clear-cut additional evidence that the sympathetic system (the term being confined to the "ortho-sympathetic" as contrasted to the parasympathetic system) is not involved in the tonic responses of "complete" Adie's syndrome. This reviewer wishes to compliment the author for a fine piece of work. He would like to take

this opportunity to emphasize that he abandoned his previously published opinion on the genesis of the tonic pupillary response (1942), to which the author refers.

In 1942, I believed the syndrome to be connected with a supra-nuclear condition (probably irritative in nature) in the diencephalon or its connections with the midbrain. During the following years, a number of clinical observations, experiments on animals and an improved understanding of basic pupillary mechanisms caused me to abandon the earlier theory. These experiments and considerations are discussed in two recent papers: (1) Miosis in Argyll Robertson Syndrome and Related Pupillary Disorders, Arch. Ophth. 1956, *55:* 356–370; (2) The Argyll Robertson Pupillary Syndrome: Mechanism and Localization, Am. J. of Ophth. 1956, *42:* 105–121. To summarize:

(1) I realized that diencephalic stimulation, intense enough to block the light reflex, would have to affect both eyes and would have to lead to maximal dilatation of the pupils (about 8–9.5 mm. in darkness). In contrast, we found that (a) in patients with a unilateral Adie's pupil, the opposite pupil was often entirely normal, and (b) the dark-adapted Adie's pupils were not excessively large. In 20 clear-cut clinical cases, the diameters of the Adie's pupils ranged from about 5 to 8 mm. and, in many of these cases the normal pupil (in darkness) was the larger one.

(2) Pupillotonia has been reported to develop in cases which, at previous examinations, had shown large and fixed pupils (Rothmann, Axenfeld, Reitsch, Adie; also Russell in one case). We observed three such cases. At the time of the first examination, the pupils were large and reacted poorly to light and to near vision. From 2 months to 1 year later, the typical pupillotonic pattern had developed, with poor reactions to light, extensive, slow contraction to near vision with delayed redilatation when the effort of near vision was relaxed. In one of these three cases, the pupillotonia was seen to gradually develop over a period of four months. X-ray examination revealed an intra-orbital tumor on the same side.

(3) A second case was seen in which an intra-orbital mass was found on the side of the Adie's pupil. Similar cases, according to Russell, have been reported by Axenfeld, Ohm, Cords, and Garcin and Kipfer.

Experiments on animals confirmed the opinions derived from these clinical facts: (1) Inhibition of the light reflex, which was produced by experimental stimulation in the diencephalon, always affected both pupils. This inhibition is a central nervous phenomenon, i.e., it takes place at the level of the oculomotor nucleus. It can still be produced after cervical sympathectomy, while the most intense cervical sympathetic stimulation will not produce the inhibition. These facts prove that the absence of light reactions and tonicity of the near vision response in Adie's syndrome cannot be explained by increased adrenergic stimulation in the iris of one eye.

(2) In experiments on the effects of peripheral (sympathetic or parasympathetic) denervation, we observed a characteristic difference between normal (neural) reactions and neuro-humoral responses obtained from completely or partially denervated effector structures which had become hypersensitive. The normal motions were fast. They accelerated to an early and high peak of speed, then gradually slowed down. In contrast, the denervated-hypersensitive responses, though often extensive, were slow and went on at at even speed. In their dynamic structure, we found the near vision contractions of Adie pupils to be the exact mirror images of the neuro-humoral dilation responses obtained when the dilatator pupillae had been rendered hypersensitive to adrenergic substances by sympathetic denervation.

(3) Finally, the demonstrable supersensitivity to cholinergic substances of typical Adie pupils, as demonstrated by Scheie's mecholyl test, can not be explained in any other

way than by a lesion (probably ganglionic or postganglionic) in the parasympathetic effector path. Here, again, the dilation responses obtained after sympathectomy show complete analogy. Supersensitivity to adrenaline develops most extensively after removal of the superior cervical ganglion or interruption of its postganglionic branches, only slightly after preganglionic peripheral sympathetic lesions, and not at all in cases in which the sympathetic pupillary innervation is disturbed centrally.

For all these reasons, I concluded that the process responsible for the typical tonic pupillary syndrome seen in Adie patients is probably located in the ciliary ganglion, leading to destruction of a majority of its cells; consequently, hypersensitivity of the iris sphincter to cholinergic substances develops and leads to slow, tonic pupillary constriction when acetylcholine is liberated by surviving fibers during the near vision reaction.

In the "complete" syndrome outlined by Adie, the "tonic" pupil was associated with diminution or absence of tendon reflexes. Adie's main emphasis was placed on the benign course and the non-syphilitic nature of the condition. When limited to such "complete" cases, the syndrome presents a clear-cut entity which can easily be diagnosed in clinical cases. But Adie extended his description to what he called "incomplete" forms of the condition; namely, (1) the tonic pupil without other symptoms, (2) atypical phases of the tonic pupil alone, (3) atypical phases of the tonic pupil with absence of deep reflexes, and (4) absent deep reflexes alone. The term "atypical phases of the tonic pupil" included the large, "fixed" pupils of internal ophthalmoplegia and iridoplegia.

The author appears to follow Adie by recognizing separate "paralytic" and "tonic" types of the condition. Other authors, among them this reviewer, object to the inclusion of cases with internal ophthalmoplegia or iridoplegia and prefer to limit the concept to (1) "complete" cases of Adie's *syndrome* (pupillotonic pseudotabes, including the tonic pupil and abnormal deep reflexes) and (2) "incomplete" cases with Adie's *pupil*, i.e., tonic pupils with normal tendon reflexes.

As mentioned above, cases were observed in which the pupil, after an earlier paralytic stage, later developed the tonic response pattern. In these cases, the large "fixed" pupil was only a transitory stage and was later proven to be an Adie pupil by the development of cholinergic supersensitivity and pupillotonia. This development allowed the localization of the lesion in the orbit. In contrast, a large, "fixed" pupil which fails to develop cholinergic supersensitivity may be due to a lesion in the third nerve nucleus or to the third nerve in its intracranial course.

As a general rule, Adie's opinion of the benign, non-syphilitic nature of the condition can be maintained for "complete" cases in which pupillotonia is combined with abnormal tendon reflexes. In contrast, internal ophthalmoplegia may be found in cases with syphilitic or other infections of the central nervous system, brain tumors and vascular or traumatic conditions.

The pathology in cases with isolated tonic pupils is not necessarily limited to inflammatory or degenerative processes in the ciliary ganglion (or its postganglionic branches), running a benign course. As mentioned above, cases were observed in which pupillotonia without other neurological signs was associated with intraorbital tumors. This fact should be borne in mind, and cases with a tonic pupil should not be considered harmless until the existence of an intraorbital tumor has been ruled out.

OTTO LOWENSTEIN

THE ORBIT

CLINICAL OBSERVATIONS OF ENDOCRINE EXOPHTHALMOS

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Brit. J. Ophth., 1956, *40:* 553–557

It is often hard to decide whether to depress the thyroid activity of a patient with endocrine exophthalmos. The importance of arriving at a correct decision, which cannot be based on the degree of protrusion alone, warrants consideration of a further useful clinical sign. The degenerative and infiltrative changes in endocrine exophthalmos are now generally agreed to be essentially the same whether or not there is obvious overactivity of the thyroid. Study of various patients with and without thyrotoxicosis suggests that the degree of orbital change may differ in accordance with changes in thyroid activity. In 1930, Birch-Hirschfeld pointed out the fact that in a normal subject a change from an upright to a recumbent position causes the globe to lie from 1 to 3 mm. deeper in the orbit. This change in the degree of occular protrusion can be demonstrated by simple exophthalmometric measurements.

Similar measurements were made in 17 patients suffering from thyrotoxicosis and exophthalmos, but without ophthalmoplegia; 7 patients suffering from exophthalmos and ophthalmoplegia, but with no evidence of thyrotoxicosis, as indicated by absence of struma and a normal basal metabolism; and 11 patients with endocrine exophthalmos, who were suffering from both ophthalmoplegia and thyrotoxicosis, as indicated by the presence of struma and an increased basal metabolic rate. In all 11 of these last patients, the thyrotoxicosis was being treated with thiouracil. A reduction in ocular protrusion similar to that found in normal subjects was dmonstrated in practically all of the patients in whom thyrotoxicosis (untreated by thiouracil) was present and who had no ophthalmoplegia. The subjects in the two other groups—in both of which ophthalmoplegia was present—did not show the normal difference in ocular protrusion when they changed from the upright to the recumbent position. If it can be assumed that the normal displacement of the globe of from 1 to 3 mm. is due to displacement of the fluid and fat content of the orbit, then the orbital fluid and fat in the patients with thyrotoxicosis without ophthalmoplegia was so little changed as to be normally displaceable. On the other hand, exophthalmos in patients with ophthalmoplegia, with or without thyrotoxicosis, seems to be due to infiltrations or changes in the orbit so severe as not to permit displacement of the fat or fluid. Measurement of the displacement, therefore, seems to provide a method of distinguishing between a "soft" and a "hard" orbit, and may be helpful in determining the measures to be taken in the treatment of endocrine exophthalmos.

The presence of a "hard" orbit in a patient with thyrotoxicosis may indicate a need for caution in the use of thiouracil or thyroidectomy.

Comment: Ophthalmologists are continually on the lookout for some treatment that may help their patients with so-called "endocrine exophthalmos." This is particularly important in those patients who are afflicted with the relentlessly progressive type of exophthalmos. The possibility of discovering some clue during the course of the disease that would help the internist to determine the correct method of treatment remains a challenging puzzle. The author by his detailed measurement of the displacement of the globe in the reclining position feels that he can determine the presence of a "soft" or "hard" orbit. The presence of a "hard" orbit, in the author's opinion, should serve as a precaution to the treatment of the thyroid component of the disease by thiouracil or thyroidectomy.

Although I see no objection to the detailed measurement of the exophthalmos in both the sitting and reclining positions by the Hertel exophthalmometer, I wonder if the examiner needs to go to such effort to determine the resistance to backward displacement of the globe. By simple palpation of the orbit in these cases the ophthalmologist can pretty well assess the degree of edema and hypertrophy of the soft tissue components. Therefore, the author's test does not seem to me to have much practical value.

That this test would have clinical application as a yardstick for determining the need of thiouracil or thyroidectomy seems doubtful. I agree with the author's implication that a "hard" orbit poses a complex problem of treatment, but I believe that the need for thiouracil or thyroidectomy should depend on the internist's evaluation of the thyroid gland rather than the ophthalmologist's determination of the displacement of the globe. The successful therapy of these "hard" orbits will have to await the discovery of all the secrets of the pituitary gland rather than depending on the manipulation of the basal metabolic rate by various thyroid drugs.

JOHN W. HENDERSON
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RADIOTHERAPY IN THE TREATMENT OF ORBITAL TUMORS

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Brit. J. Ophth., 1956, *40:* 592–610

The clinical material on which this study is based cannot fairly be used for assessing the incidence of orbital tumors, because it was selected according to the therapy required. Furthermore, because it was so selected, it contained a large preponderance of secondary malignant tumors, 126 as against 42 that were primary. Benign tumors were present in 17 patients and 5 had granulomas (3 of which were malignant).

The indications for radiotherapy in benign tumors are restricted to hemangiomas. These tumors often regress spontaneously in children, but when treatment is indicated, radiotherapy is the treatment of choice. It is safe because only

infrequent small doses are necessary, but, whereas results in lid and cutaneous hemangiomas are almost uniformly satisfactory, complete resolution is not invariable in orbital cases, and surgical removal after radiotherapy was necessary in one of the patients.

Malignant granulomas are necrotizing processes of unknown cause generally affecting the nasal passages. The outcome is usually fatal and the only remedy of occasional but proved value is radiotherapy. Three of the six patients seen had proptosis in addition to invasion of the nasal fossa and paranasal sinuses, and in two the eye was lost.

The diagnosis of a primary malignant orbital tumor must be confirmed histologically. Histological confirmation was obtained in all but one of the 42 such tumors in this series, and in none of the patients was the local condition made worse as a result of the biopsy. The primary tumors seen by the radiotherapist are those regarded as unsuitable for operation, i.e., sarcomas of lymphoid tissue, other rapidly growing sarcomas in children and young adults, and malignant lacrimal gland tumors that cannot be totally removed.

Sarcomas of lymphoid tissue are the commonest primary orbital tumors; they are all uniformly radiosensitive and radiotherapy is the treatment of choice. The reticulosarcoma is the least malignant of the group and has the best prognosis, whereas in lymphosarcomas and benign lymphomas wide dissemination sometimes occurs or a leukemic blood picture develops, or again the patients sometimes remain well for a variable period. The results in the 14 patients with tumors belonging to this group show that the prognosis is reasonably good; none of the eyes was lost through radiation treatment.

The present experience with rhabdomyosarcomas in the 7 patients with this rare tumor seems to show that they occur mostly in children, remain localized in the orbit, and are highly radiosensitive. They are, however, only exceptionally radio-curable, since prompt recurrence is nearly always the first rule. Radiotherapy, however, should be used in the first instance. There is no evidence to show that immediate exenteration has any advantage and as the tumors appear to remain localized, any delay in operation because of the preliminary attempt at cure by radiotherapy seems not to be associated with an increased risk of metastases. In the four patients who died of this disease, distant metastases were not demonstrated, although it must be conceded that post-mortem examinations were not made. Three patients have survived, one for 3 years, one for 1½ years, and one for about 6 months.

Lacrimal gland tumors vary widely, both in structure and in clinical behavior. However benign the histological picture, these tumors should always be regarded clinically as malignant. With the so-called mixed tumors of the lacrimal gland, the tempo of recurrence and spread is usually more rapid than with the corresponding tumors of the main salivary glands to which they seem to be analogous, and the prognosis is therefore much graver. Reese (1951) attributes the high proportion of recurrences and the high mortality from lacrimal gland tumors to the difficulties of surgical approach and removal, the tendency to invasion of the capsule, and particularly the early invasion of bone. Radiotherapy can help

to reduce the recurrence rate within the limitations and fallacies imposed by the 5-year period of observation in these tumors with their characteristic slow remorseless progress, and it should therefore be used routinely in association with surgery. Radiotherapy is, of course, the method of choice for the inoperable, recurrent, or highly malignant epithelial tumors and the lymphosarcomas.

Only two 5-year survivals were obtained in patients with other malignant tumors; in these cases, the growths were a glioma of the optic nerve and a liposarcoma.

The 126 secondary malignant tumors in this series include 6 intraocular tumors, 100 tumors arising in neighboring regions, 10 metastases from various sources, and 10 orbital manifestations of generalized lymphoid tumors. Malignant intraocular tumors are usually treated by removal of the affected eye. Radiotherapy is reserved as a postoperative measure if examination of the excised eye shows evidence of extraocular spread, or if frank postoperative recurrence is detected in the socket or orbital cavity after exenteration. Orbital metastases should be treated by radiotherapy if the patient's general condition is satisfactory; otherwise, the patient may live long enough to develop the distressing symptoms associated with progressive and uncontrolled proptosis and his terminal state may become truly wretched. Secondary deposits of this type respond reasonably well to radiotherapy, and the patients can usually be spared removal of the eye or more radical orbital surgery.

Secondary extension to the orbit from primary cancers of the lid and epibulbar region should be treated by radiotherapy, followed by radical surgery whenever possible. Radiotherapy alone is usually of palliative value only, and surgery without radiotherapy is likely to be followed by recurrence.

Radiotherapy is the treatment of choice for orbital lesions occurring during the course of an already established and generalized lymphoid tumor.

The most common secondary orbital tumor seen by the radiotherapist follows invasion of the orbit from a paranasal sinus cancer, or from the postnasal space. This process is always of grave significance for prognosis and adds to the technical difficulties of treatment because of the need to avoid radiation damage to the eye. Removal of a sound eye or exenteration of the orbit is never justifiable as a primary measure in the treatment of antral or ethmoidal cancer, for it adds little to the patient's chances of survival. The presence of neoplasm in the orbit is an index of the extensive nature of the disease and if radiotherapy is used and fails, subsequent surgery is not likely to succeed.

In advocating radiotherapy for the treatment of malignant orbital tumors, the possible risks of damage to the normal eye must be kept in mind. If the risks are considerable, then a case can be made out for removing the eye before embarking on radiotherapy, but if the risks are small or otherwise worth accepting, the eye should be left, since it is far better for a patient to retain the eye even at the cost of impaired vision than to suffer its removal, which is inevitable when a malignant orbital tumor is treated surgically.

The risks of radiation damage to the eye depend on the radiosensitivity of the tumor and the dosage employed, the state of the eye before treatment, the tech-

nical method employed, and the degree of protection possible. Radiation cataract is by far the commonest single complication and is to be expected in nearly all malignant cases treated. There is usually a latent period of about 3 years between the treatment and the onset of the cataract, which as a rule occasions surprisingly little complaint. It is justifiable to run the risk of radiation cataract when there is no alternative to radiotherapy or when surgical treatment would entail enucleation.

Other ocular complications are superficial punctate keratitis, corneal ulceration, disturbance of lacrimal secretion, vitreous hemorrhage, epilation of the lashes and brows, scarring, and socket contraction.

A good eye should never be sacrificed for the sake of technical expediency or fear of postradiation complications, but a blind eye that has already been damaged or an eye that is proptosed and affected by a severe exposure keratitis, neuroparalytic keratitis, or panophthalmitis should be removed as a preliminary measure. In dealing with radiosensitive tumors, even a severely damaged eye may be saved, and this should always be borne in mind when a patient is reluctant to agree to its removal.

The greatest safeguard to the eye is to shield it against radiation either direct or indirect. The vulnerable part of the anterior segment should be shielded in all cases, and the sound eye should be completely shielded, however slight the apparent risk. Local contact methods of gamma radiation using radioactive sources near the normal eye should be avoided. Local tissue reactions can be controlled in part by attention to the dosage and time factor.

Comment: This article is written by a radiologist. The author reviews a large series of orbital tumors which were collected from several hospitals and which were treated by radiotherapy. From the standpoint of this review, it would be convenient to divide the article into two parts. The "first part" details the author's experiences and beliefs concerning the effect of radiotherapy on various neoplasms and granulomas. This is the part of the article that would be of most interest to an ophthalmologist, and this reviewer's comments will be devoted to this section. Although the "second part" would be of most interest to radiologists, it could also serve as instructive reading to those ophthalmologists who advocate administration of high dosages of x-ray to the orbit, or become impatient with the slow and delayed effects of the more conservative dosages recommended by experienced radiologists.

In the first part of the article the author's viewpoints concerning the effectiveness and rationale of radiotherapy in various orbital conditions pretty well coincides with the average opinion of ophthalmologists in this country. Only in the sections devoted to the discussion of rhabdomyosarcoma and secondary invasion of the orbit by malignancies of the eyelid does there seem to be a basis for a difference in opinion.

It is the author's opinion that rhabdomyosarcomas are radiosensitive, whereas Reese, in the United States, and Duke Elder, in England, consider these malignancies to be radio-resistant. The author details several instances wherein the administration of x-ray brought about a remission in the progress of the neoplasm as well as an amelioration of symptoms. The author is quick to point out, however, that recurrences are nearly always the rule and that in the final analysis these malignancies are not radiocurable.

It is this reviewer's impression that all of the observers, including the author, who have

reported their observations on proven cases, are in basic agreement that the majority of children afflicted with rhabdomyosarcoma do not survive no matter what treatment is employed. The apparent difference in opinion as regards the effect of radiotherapy may, therefore, revolve around the interpretation of the words "radiosensitive" and "radioresistant." If it is assumed that Reese as well as Duke Elder used the word "radioresistant" in the sense that the lesions were not radiocurable although recognizing the fact that radiotherapy could bring about some temporary improvement, and so long as the author carefully differentiates between the words "radiosensitive" and "radiocurable," then the apparent differences are reconciled.

In my own experience, I would be most prone to advise exenteration of the orbit as the preferred treatment for this type of malignancy.

In his discussion of the management of malignancies that invade the orbit secondary to involvement of the eyelid, the author reiterates a belief commonly held by radiotherapists, namely: "Extension to the orbit from primary cancers of the lid and epibulbar region should be treated in the first instance by radiotherapy, and this should be followed by radical surgery whenever possible." Most ophthalmologists and plastic surgeons would tend to argue that the radical surgery should be performed first.

The difficulty in treating these situations first by radiotherapy is that the patients, by reason of their broad endowment with the traits of human nature, tend to defer the radical surgery because the radiotherapy brings about a temporary improvement. This procrastination often allows a creeping and invisible spread of the lesion to the point where even radical surgery is incapable of encompassing the boundaries of the malignancy.

Nowadays I think these spreading malignancies are best handled by pathologists by wide excision, supplemented by frequent frozen tissue studies of samples of tissues taken from the margins of the lesions at the time of surgery so as to permit the surgeon to accomplish a complete removal verified by histologic study.

JOHN W. HENDERSON
ROCHESTER

THE RETINA AND VITREOUS

RETINAL CHANGES AND FETAL PROGNOSIS IN THE TOXEMIAS OF PREGNANCY

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Obst. & Gynec., 1956, *8:* 426–431

In the toxemias of pregnancy, it is essential to consider the fate of both the mother and the fetus. The course of the disease in the mother can be followed by observing the changes in her blood pressure, albuminuria, edema, and blood chemistry. The effects of the toxemic process on the mother and on the fetus, however, are not parallel, and the changes in the mother's symptoms do not always reliably indicate the fate of the fetus. At times the mother will be in danger because of an increasingly severe toxemia, and yet the fetus may not suffer at all. Again, there are cases in which the toxemic process shows improvement and, so far as the mother is concerned, the pregnancy may be allowed to proceed to term. Sometimes, however, there is a danger to the fetus that may lead to intrauterine death and a difficult clinical situation then arises. A lack of improvement in the mother's condition makes termination of the pregnancy desirable, but because the fetus may not yet be viable, there is a tendency to wait. It is during this waiting period that there is danger of intrauterine fetal death.

A study was therefore made to see if frequent examination of the ocular fundi, in addition to other routine investigations, would be helpful not only in the evaluation of the mother's condition but also of the fetal prognosis. During the period from January, 1952, to July, 1955, there were 176 cases of toxemia of pregnancy (188 fetuses including twins) out of a total of 7976 deliveries, an incidence of 2.2 per cent. There was no maternal mortality. Classification of the toxemic conditions in these patients according to Dieckmann's criteria showed that 110 were mild and 51 severe, these last being the preeclamptic, eclamptic, and hypertensive conditions. The remaining 15 were cases of renal disease.

Analysis of the findings showed a correlation between the vascular changes in the retina and the degree of severity of the toxemic condition. The proportion of severe cases of toxemia increased progressively and the proportion of mild cases decreased as the retinal changes became more severe. A close correlation was also found between the retinal changes and the fetal mortality rate. As the retinal vascular changes became more severe, the danger to the fetus became correspondingly greater, as shown by the increasing incidence of fetal mortality.

In cases of mild toxemia with grade 2 retinal changes, the fetal mortality rate was 22.2 per cent, whereas in cases of severe toxemia with grade 2–4 changes, this rate was doubled. Similarly, the fetal survival rate declined as retinal changes became more severe in patients with chronic renal disease. There were, however, no fetal deaths in either mild or severe cases in which retinal changes were lacking.

Taking into account the poor fetal prognosis in all cases of severe toxemia with grade 2–4 retinal changes, termination of the pregnancy should be seriously considered even though the fetus may not be viable; it may be that emphasis on the good care of the premature infant will reduce the fetal mortality rate in the toxemias of pregnancy. In any case, the results of this study show that frequent examinations of the retina in patients with toxemia of pregnancy are undoubtedly helpful in the evaluation of fetal prognosis and the management of the disease.

Comment: Since the Keith-Wagner classification, as applied to fundi in toxemia of pregnancy, indicates mainly the degree of arteriolar spasticity and its complications, viz., a functional state which is largely reversible unless the picture is complicated by a preceding renal or hypertensive disease, it is obvious why there is such parallelism between the degree of observable retinal vascular changes and fetal mortality.

The critical point in evaluating the positive fundus findings of any degree lies in their duration. Prolonged moderate arteriolar spasticity which has not yet led to retinopathy may be as detrimental to the fetus as a more pronounced spastic condition with marked retinopathy or neuroretinopathy of short duration. Thus, a greater responsibility seems to rest with the ophthalmic consultant who is called upon to interpret the moderate rather than the severe degrees of retinal participation.

Repeated fundus examinations by the same examiner during the period of waiting for a viable age of the fetus, especially in the mild toxemias and in the more severe ones which respond well to therapy, should prove most fruitful in reducing maternal and fetal complications.

BERTHA A. KLIEN

ROLE OF A DISTINCTIVE CHOROIDORETINAL LESION IN THE PATHOGENESIS OF RETINAL HOLE: A CLINICAL AND PATHOLOGICAL REPORT

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Brit. J. Ophth., 1956, *40:* 527–535

A retinal hole is now generally accepted as the immediate and causative precursor of retinal detachment. Hole formation, however, is not the primary lesion, but is rather the result of degeneration, usually cystoid in type, or of atrophy of

the retina. Possibly a disturbance of the vitreous also precedes hole formation, local fibrillar attachments of the vitreous being capable of disrupting the remaining fine inner layer of the retina.

The retinal degeneration or atrophy and the local vitreous changes are in turn probably not primary changes. The retinal condition depends on the nutritional supply, which comes from two sources—the chorio-capillaries and the retinal capillaries. Among the various factors that may affect this supply are choroidoretinitis leading to obstruction of the capillaries of both choroid and retina. In this connection, a distinctive choroidoretinopathy was described by the author (1955) as frequently present in the neighborhood of retinal holes. This choroidoretinopathy, which is characterized by local pigment disturbance of the choroid and by phlebosclerosis in the overlying retina, precedes the visible retinal changes.

Four further cases in which a retinal hole was associated with the characteristic pigmentary changes and sclerosis of the retinal vessels are now presented, together with the histological findings in one, in which the eye was removed because of choroidal sarcoma. The occurrence of a retinal hole in this eye seems inexplicable. That it was fortuitous was clear from the relative positions of the hole and the detachment caused by the tumor. The histological findings in this case support the clinical findings and add the following facts to the clinical description of the choroidoretinopathy under discussion: (1) The local choroid is atrophic and its vessels are almost obliterated; (2) some of the pigment noted ophthalmoscopically is seen to be intraretinal; (3) the sheathing of the local vessels is due to a hyaline degeneration; (4) fibrillar disturbance is visible in the local vitreous; and (5) more holes may be present than are clinically noted.

From these findings it appears that, in the pathogenesis of certain retinal holes, an atrophic pigmented choroidopathy is associated with a local retinal phlebosclerosis and a fibrillar disturbance of the adjacent vitreous. These changes give rise to an atrophy of the retinal tissues, which may be torn by the pull of the altered and adherent vitreous fibrils. The prerequisites for hole formation diversely postulated or emphasized by various authors on theoretical, clinical, and histological grounds are apparently supplied collectively by a single distinctive choroidoretinopathic process. This process, which seems to meet the two prerequisites for degeneration and atrophy of the entire thickness of the retina—that is, closure of the local chorio-capillaries and closure of the local retinal vessels—is apparently accompanied by a simultaneous degeneration of the local vitreous.

The cause of the process may be a general disturbance not confined to the eye. This possibility will be dealt with in a later publication.

Comment: The triad of clinical findings of localized retinal phlebosclerosis, pigment migration into the retina and adjacent retinal hole formation has been subjected to comment in this publication before (F. Graupner, Zentralbl. ges. Ophth. 1955, *65:* 323, Survey Ophth. 1956, *1:* 350). The author's assumption that the pigment migration represented the end result of a choroidal process, coexisting with the retinal lesions, was discussed and questioned.

The present author adds several clinical observations of this triad and one histologically studied case. The sclerosis of retinal vessels, shown in the histologic specimen, the circumscribed extreme atrophy of the retina surrounding the hole, and a vitreo-retinal adhesion, which had caused splitting of the retina (see also Klien, Am. J. Ophth. 1955, *40:* 515: Concerning the Pathogenesis of Retinal Holes) seem quite sufficient for production of a hole without additional choroidal process.

The histologic findings in the trephined piece of shrunken, formalin-fixed, peripheral choroid are very unconvincing, and your commentator still believes that this interesting, important triad of findings is produced by a purely retinal process.

BERTHA A. KLIEN

ECTOPIA OF THE MACULA

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Brit. J. Ophth., 1956, *40:* 492–496

Ectopia of the macula, found in three patients aged 12 years, 20 months, and 34 years, recently seen at the Royal Eye Hospital, is a striking clinical condition. Only 14 cases have previously been reported, although 8 specimens in which the diagnosis was made histologically after perforating injuries were described by Fuchs in 1921. The appearance of the fundus in the first two of the authors' patients suggested that an abortive retrolental fibroplasia might have been responsible for the macular displacement. In the third patient, it was almost certainly due to cicatricial contraction of the retina following retinal periphlebitis.

Most of the recorded cases have been attributed to a developmental anomaly at the posterior pole of the eye. This would appear to be the most probably explanation in the two patients recorded by Triebenstein (1919), a mother and son with very similar fundus appearances, and also in another case quoted by him which was associated with familial microcephaly and microphthalmos. He also mentions four cases of ectopia of the macula with associated pigmented choroidal lesions, colobomata, anomalies in the distribution of the retinal vessels, or bands in the retina or the vitreous. These were all apparently congenital and presumably developmental anomalies, though it is often impossible to distinguish between intrauterine inflammatory lesions and developmental defects. The description of the fundus lesions in some of these cases is reminiscent of the appearances in the authors' first two cases, and it is possible that some of them were due to retrolental fibroplasia. In only three of the recorded cases was the condition known to be acquired: in one it followed a blow to the eye; in another it developed after an operation for divergent strabismus; and in the third the macula in a tuberculous patient who had had a retinal detachment nine months earlier was found to be drawn downwards by traction bands.

It is perhaps surprising that the macula is so rarely displaced after the reposition of extensive retinal detachments, and it may be that the circumstance responsible for such displacement is a widespread inflammatory process involving the retina alone, rather than one restricted in area but extensive in depth, such as follows the surface application of diathermy to the sclera.

Comment: For the interesting condition of a progressive displacement of the macular region the term dislocation of the macula would be more appropriate than that of ectopia of the macula. The latter should be reserved more or less for a congenital anomalous condition, which, in a mild degree, is not as rare as the paucity of reports in the literature would indicate. Obviously only very marked degrees of it are reported.

The milder degrees are often associated with an anomalous distribution of the retinal vessels, viz., large branches running close to the fovea centralis, an unusually small avascular central area, or a large upper branch crossing the normally avascular area downward to supply part of the inferior fundus, and many others.

The acquired condition is much more interesting, especially when encountered in an adult such as the author's third case. In this 34-year-old man with retinal periphlebitis in the inferior temporal periphery of one eye, two fundus pictures made five years apart, illustrate well the progression of the displacement of the fovea centralis.

In the second picture the fovea is not only lower but also almost one disc diameter further away from the disc than in the first picture, with more distortion of the disc and more pronounced straightening of the vessels. It is regrettable that there is no record of successive tests of vision during the 5-year period, only the initial vision of 6/12 being mentioned.

The visible dislocation must be affected mostly in the inner layers of the retina at the site of the second and third neuron. A marked dislocation might also affect the percipient retinal elements, to what an extent, tests of visual acuity would show.

With a vision of 6/12, this condition is of necessity only a partial displacement of the macula, namely its inner layers, and not well described by the term ectopia.

BERTHA A. KLIEN

SYSTEMIC DISEASE

LEPTOSPIRAL UVEITIS: REPORT OF FOUR CASES DIAGNOSED IN FINLAND

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Acta ophth., 1956, *34:* 185–194

Ocular manifestations in leptospirosis are both frequent and various. In the acute febrile phase conjunctivitis and episcleritis commonly occur as diagnostically significant symptoms manifested as hyperemia. Other eye symptoms occurring in the acute stage are light sensitivity, papillary hyperemia, yellowness of the conjunctiva in jaundice, and hemorrhages into different parts of the eye in hemorrhagic diathesis. In addition, there are descriptions of various pupillary changes in connection with leptospirosis (mydriasis, anisocoria), ptosis, paralysis of the ocular muscles, papillary edema in association with serous meningitis, and fairly often optic neuritis. The most important eye symptom, however, is uveitis. This symptom may appear as early as at the end of the acute febrile stage but it usually becomes evident only after a symptom-free interval of a few weeks' or months' duration.

Leptospiral uveitis presents such a characteristic appearance that its true cause is at once suggested on slit-lamp examination. Among the typical findings are a slightly hyperemic iris, fine-grained visible aqueous flare, slight, often persistent precipitates, and posterior synechiae easily detachable by mydriatics. In the more severe chronic form of the disease membranate opacities of the vitreous are frequently seen, as well as so-called vitreous precipitates. Leptospiral uveitis is usually unilateral, or inflammatory symptoms may predominate in one eye; inflammation, however, often migrates from one eye to the other, and relapses are also common in one and the same eye.

The various forms of the disease have been described as acute mild iridocyclitis without notable vitreous opacities; severe slowly improving iridocyclitis, with membranate vitreous opacities characteristic of the disease; and recurring iridocyclitis, which is considered rare. In addition, there are said to be a fibrinous form, which is acute and often appears in the febrile stage, and a serous form, which has a later onset and milder symptoms.

During recent years success has been achieved in demonstrating living leptospirae in the fluid of the anterior chamber in association with uveitis, after the clearing up of the acute febrile stage. Present indications are that leptospiral uveitis is caused by the presence of leptospirae and by the allergic and toxic changes produced by them.

Interest in this condition has only recently been aroused in Finland and the four cases presented by the authors are the first to be diagnosed in that country. The diagnosis was based in the first place on the positive titers found in the leptospiral agglutination lysis test. The leptospiral types responsible were L. bataviae in two patients, L. sejroe in one, and L. poi in one. The cases of uveitis caused by L. sejroe and L. poi are probably the first to be published in the literature as being due to these types. Clinically, the cases primarily resembled the form of acute mild leptospiral uveitis. Three of the patients exhibited so-called roseola formations in the iris at the acute stage of the disease. Uveitis was unilateral in two cases. One patient was given aureomycin by mouth without any particular effect on the course of the disease. Local atropine and hydrocortone therapy resulted in fairly rapid improvement without visual impairment. There were no relapses.

These cases of leptospiral uveitis were found in a group of 66 patients being treated for iritis and uveitis. Their discovery seems to show that the presence of leptospiral antibodies in the blood should be investigated, at least in clinically doubtful cases of uveitis. While it is true that such an investigation does not essentially affect the treatment of the disease, it may help to elucidate its true etiology and prevent useless therapy of long duration, because, for instance, the picture of leptospiral uveitis sometimes resembles that found in tuberculous uveitis.

OCULAR MANIFESTATIONS OF RILEY-DAY SYNDROME: FAMILIAL AUTONOMIC DYSFUNCTION

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A.M.A. Arch. Ophth., 1956, *56:* 719–725

The syndrome of familial dysautonomia, first described by Riley and co-workers in 1949, is becoming of increasing interest to both the pediatrician and the ophthalmologist. Although the number of cases on record is still comparatively small, the disease is probably not rare. Riley himself knows of more than 70 that meet his criteria.

The syndrome is characterized by a plethora of symptoms. The earliest manifestations in infancy may be retarded development with low weight gain, difficulty in swallowing, and frequent bouts of respiratory infection or aspiration pneumonia with an exaggerated febrile response. The infant is subject to dehydration and may perspire and drool excessively. He fails to produce tears when he cries. With a few exceptions, the cases reported have occurred in Jewish

children. The physical examination reveals generalized indifference to pain, including corneal hypesthesia; hyporeflexia; labile hypertension, and postural hypotension.

Three cases, representing different degrees of corneal involvement, are reported in this paper for the purpose of providing a more complete picture of the ocular manifestations of this disease. Case 1, in which the postmortem findings, including the ocular pathology, are recorded for the first time, represents the severe ulcerative type. Cases 2 and 3 are examples of the minimal, easily overlooked, and more frequent types of keratopathy not previously described.

The first patient was a Jewish boy born Jan. 30, 1951, weighing 5½ lb. He was in medical difficulty almost constantly until his death, two years later. Corneal ulceration developed in both eyes and was treated by tarsorrhaphy. Tongue-biting became so serious that several teeth had to be extracted. Finally, on March 9, 1953, without warning, the child was found dead in its crib. The general pathological diagnoses immediately after death were bronchopneumonia, confluent, bilateral, extensive; lacerations of the tongue; bilateral double ureters and pelves, and multiple tooth extractions. The pancreas was normal. The ocular involvement in this patient was so severe that it resembled neuroparalytic keratitis and keratomalacia. Pancreatic fibrosis with secondary vitamin A deficiency and keratomalacia can produce a similar picture, both in its systemic and in its ocular manifestations, and the postmortem findings, though nonspecific, were useful in ruling out a diagnosis of pancreatic fibrosis, which had at one time been considered. The findings on microscopic examination of the ocular tissues were also nonspecific, merely showing evidences of severe keratinization and ulceration without inflammatory reactions. The fact that the findings were nonspecific is not surprising in a disease thought to be due to a disturbance of neurologic function.

The corneal involvement in the second patient, a Jewish girl weighing 5 lb. 5 oz. at birth, who had various episodes of infection, fever, and dehydration leading to a diagnosis of familial dysautonomia, was almost entirely in the lower one-third of the cornea. It responded very readily to simple local treatment. The residual scarring is slight and could easily be overlooked on casual examination. When active, however, the lesion was obvious and of such a character that it could never have been confused with keratomalacia or neuroparalytic keratitis. The child's parents have been instilling a bland ointment into each eye every night and have been advised to increase the instillations to three a day if and when bouts of fever and dehydration occur.

The third patient, a Jewish boy born normally at term, was admitted to the Children's Hospital 20 times, mostly for bronchopneumonia, tonsillitis, and pharyngitis with hyperpyrexia and dehydration. Between the fourth and fifth admissions, he was given a diagnosis of familial autonomic dysfunction. Notwithstanding examinations by numerous members of the resident and visiting staffs during these 20 hospital admissions, ocular involvement was never noted. He was first seen at the age of 3 years by the author. Definite irregular superficial scarring in the lower one-fifth of the right cornea and faint scarring of the

left cornea were observed. This child thus presents an example of the minimal type of corneal involvement, in which the ocular symptoms do not necessarily come to the attention of either the parent or the pediatrician but are observed only on ophthalmologic examination, with use of focal illumination with magnification. Such lesions are important diagnostically and therapeutically. They indicate that the corneas are vulnerable and suggest that prophylaxis, in the form of a protective ointment instilled at night, is needed.

These cases show that the ocular abnormalities in the Riley-Day syndrome (familial autonomic dysfunction) may appear as (1) a severe central ulceration resembling neuroparalytic keratitis and keratomalacia, responding only to tarsorrhaphy; (2) a mild process resembling exposure keratitis in its location and appearance, responding readily to the instillation of a protective bland ointment or to saline eye drops; and (3) a faint scarring resembling etched glass in the lower cornea occurring in the absence of any history of ocular symptoms or disease.

Comment: Since its recognition and description in 1949, the Riley-Day syndrome has proved more common than originally suspected. This familial syndrome is manifested in infants by multiple autonomic dysfunctions including emotional instability, hypesthesia, labile hypertension, excessive perspiration, poor temperature regulation, difficulty with swallowing, dehydration, frequent respiratory infections and retarded motor and mental development.

Ocular signs of this syndrome result from lack of tears and corneal hypesthesia. As demonstrated in this paper, variable corneal damage may result. As pointed out by Dunnington, the normal appearing conjunctiva distinguishes the ocular findings from keratomalacia. The bilaterality and normal trigeminal nerve permit differential diagnosis from neuroparalytic keratitis. Recognition of the Riley-Day syndrome by pediatricians and ophthalmologists and awareness of its ocular complications may permit protection of the cornea by tarsorrhaphy.

BERNARD BECKER

THERAPEUTICS

RESULTS OBTAINED IN THE TREATMENT OF UVEITIS WITH CORTISONE (FIVE YEARS' EXPERIENCE)

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Arch. opht., 1956, *16:* 261–273

Since 1950, 150 patients with acute and chronic uveitis have been treated with cortisone in the Ophthalmological Service of the Hôpital Cochin. These cases were distributed as follows: 110 chronic iridocyclitis, 20 choroiditis, and 20 acute iridocyclitis. Under the heading of chronic uveitis are included all the cases in which the disease had lasted more than 6 weeks and in which, after apparent sedation, there had been one or more relapses. Localization of the disease in either the anterior or the posterior segment was associated in a large majority of the cases with involvement of the vitreous, which, when present, is a very important element from the point of view of prognosis.

The 110 cases of chronic uveitis comprised 4 of rheumatic iridocyclitis, 20 of iridocyclitis of focal origin, 5 of Fuchs' syndrome, 7 of tuberculous uveitis, 6 of menopausal uveitis, 3 of uveitis associated with interstitial keratitis, 1 of spirochetal uveitis, 16 of sympathetic ophthalmitis, 12 of post-traumatic uveitis, and 36 for which no cause could be found in spite of intensive investigation.

Cortisone was used in most patients, although a few were given hydrocortisone and ACTH was used when cortisone by the general route was contraindicated. Treatment with these hormones should always be accompanied by antibiotic treatment because of the danger presented by infections that develop during hormone therapy. Moreover, since cortisone is not an etiologic remedy, it should always be accompanied by specific therapy when the cause of the uveitis is known.

Analysis of the results obtained in these cases shows that cortisone was highly effective in acute iridocyclitis, restoring the tension to normal in 60 per cent of the patients with hypertensive uveitis. It was less effective in chronic uveitis: the results were slight in menopausal uveitis, and poor in Fuchs' syndrome and certain cases of rheumatic iridocyclitis. Moderate results were obtained in allergic tuberculous uveitis and uveitis of focal origin. In uveitis of unknown origin, improvement was obtained in 50 per cent of the cases, but relapses were especially frequent because of the lack of etiologic treatment.

The best results were obtained in post-traumatic chronic uveitis, iridocyclitis accompanying interstitial keratitis, and sympathetic ophthalmitis.

Unfortunately, excellent initial results are not infrequently followed by relapse when treatment is suspended; consequently, maintenance therapy should be continued under strict medical supervision to control the often inexorable progress

of chronic uveitis and to delay if not to prevent the blindness that so frequently threatens these patients.

Comment: After the advent of the dramatic effects of local steroids in uveitis, studies of cases observed for several years are beginning to demonstrate less enthusiastic results. This survey by Offret and Haye demonstrates the inadequacy of steroids in many cases of uveitis; for example, that associated with menopause, chronic arthritis and heterochromia. Their best results were obtained in post-traumatic chronic uveitis, iridocyclitis accompanying interstitial keratitis, and sympathetic ophthalmitis but, even in these, they were impressed with the frequency of relapse. Klauder and his associates, Woods and others have previously stressed the frequency of relapse associated with the use of steroids in the treatment of interstitial keratitis and associated uveitis. Previous experience with the treatment of sympathetic ophthalmia has also demonstrated the necessity of long and continued treatment and careful, close observation in order to detect signs of recurrence. The present study confirms these findings.

Similarly, these authors confirm the value of the anti-inflammatory action of the steroids for lowering elevated pressure associated with uveitis.

The value of steroids in uveitis of tuberculoprotein hypersensitivity origin has not been established. Lurie and Zapasodi, in the treatment of experimental systemic tuberculosis, and Woods and his co-workers, in ocular tuberculosis, have demonstrated that uveitis due to active tuberculosis will flare excessively when steroid therapy combined with antituberculosis chemotherapy has been discontinued. It is of unusual interest to note that Offret and Haye have treated cases of uveitis suspected to be due to tuberculoprotein hypersensitivity successfully with steroids alone. It is difficult to establish the diagnosis of uveitis due to tuberculoprotein hypersensitivity and it is even more difficult to be certain that the uveitis, if associated with tuberculoprotein hypersensitivity, does not have an accompanying tuberculous infection. The fact that their cases did respond favorably might be further proof of the accuracy of their diagnosis. However, caution should be followed if one can not be certain of this specific etiology.

Approximately one-third of their cases were undiagnosed from an etiologic standpoint. This represents, according to most series, a high incidence of specific diagnosis. The majority of their cases were of focal origin which did about as well with treatment of uveitis as those cases which they were unable to diagnose specifically from the etiologic point of view. One can not help but be impressed with the large number of eyes with sympathetic ophthalmia in this series. Their high incidence of successful results in post-traumatic uveitis confirms that previously reported in this country by many observers.

More studies of this type which will evaluate the use of steroids in uveitis over a long period of time will be helpful in definitely establishing the position of these anti-inflammatory agents in this type of ocular disease.

IRVING H. LEOPOLD

TREATMENT OF UVEITIS WITH PYRIMETHAMINE (DARAPRIM)

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Brit. J. Ophth., 1956, *40:* 577–586

Attempts to diagnose toxoplasmosis by serological methods in patients with acquired choroidoretinitis are complicated by the widespread occurrence of low titer antibodies in normal persons. In an analysis of 200 cases, however, Smith and Ashton (1955) found that antibodies were present in their patients in a higher proportion than in the normal population. They concluded that, although titer levels were not diagnostic in individual cases, they did show a striking association between toxoplasma infection and posterior uveitis, and they suggested that one of the means of elucidating the exact nature of this relationship might be by means of the response to a specific chemotherapeutic agent.

The most suitable agent for such a trial seemed to be pyrimethamine (Daraprim) a drug first introduced for the treatment of malaria. The advantage of this substance in evaluating treatment is that it has a low antibacterial activity and, so far as is known, no effect on allergic conditions; hence, any improvement in a case as a result of treatment with this drug will almost certainly be due to its effect on the parasites.

In a preliminary report on the use of Daraprim in uveitis, it was shown that mice could be protected from the lethal effects of toxoplasmic infection by Daraprim. The results in the first 63 cases of uveitis in the clinical trial described in this paper were also reported, and it was suggested that some cases with a positive dye test were improving more rapidly than were untreated cases, although this result was not statistically significant. A further 101 cases have now been studied and the preliminary results have been confirmed at a higher level of statistical significance.

The effect of Daraprim on the 66 toxoplasma negative cases will be considered first, as it is important to show whether Daraprim has any nonspecific effect on uveitis. Of these patients, 29 received Daraprim and 37 were given control tablets containing an inert substance. Analysis of the results showed that there was no significant difference between the two groups, indicating that Daraprim has little effect in cases with a negative toxoplasma reaction.

The improvement rate in the patients with a positive toxoplasma reaction (as judged by a dye-test titer of 1 in 4 or over) treated with the control tablets was very similar to that in the patients with a negative toxoplasma reaction, both treated and untreated. A marked deviation from this improvement rate was found only in the patients with a positive toxoplasma reaction who were treated with Daraprim. In these, improvement occurred in 76 per cent, as against 56 per cent of the control group. This difference is significant by the chi square test.

The results suggest very strongly that toxoplasmosis is a causative factor in some 25 per cent of cases of uveitis with a positive dye test. This in itself is a finding of great interest and importance, but it is not of much help in the diagnosis of any single case. Some indications of the criteria that should be adopted for the diagnosis of toxoplasmic uveitis may, however, be deduced from the data. Thus, a high incidence of positive dye tests (79.3 per cent) was found in the patients with posterior uveitis as compared with those who had anterior uveitis, in whom the incidence was 59.2 per cent; the dye-test titers also tended to be higher in the group of patients with posterior uveitis than in any of the others. The best response to treatment was also obtained in the posterior uveitis group, in which the typical lesion was an area of focal choroidoretinitis with marked vitreous haze. Although no attempt was made to grade the degree of improvement, some patients showed such a marked response that the fact was noted. Notations of marked improvement were found in 6 out of the 17 cases of posterior uveitis treated with Daraprim, as compared with only 5 out of 33 cases of anterior uveitis—more than double the percentage.

Daraprim administration should be accompanied by regular blood examinations in order to detect macrocytic anemia (which occurs in some patients) at an early stage. If anemia appears and is found to be progressive, it may be wiser to discontinue the course, or to give the drug alternatively with folic acid, which does not seem to interfere with the antitoxoplasmic effect of Daraprim. Folic acid was not used in this investigation, and discontinuance of Daraprim became necessary in only one case.

Comment: This carefully controlled study by Perkins, Smith, Schofield, and members of the Uveitis Clinic with pyrimethamine (Daraprim) of uveitis is encouraging. If Daraprim has no therapeutic action other than its toxoplasma effect, these studies suggest strongly that toxoplasma is an etiologic factor in a large percentage of cases of uveitis. In the present series, it was approximately 25 per cent.

The study suggests that toxoplasmosis produces a posterior uveitis rather than an anterior one. The posterior cases had higher titers than the anterior ones. However, the cases which responded best to Daraprim therapy were those with low dye-test titers. This may indicate that a low dye-test titer is as significant as a high titer in the diagnosis of the disease or that the drug is not producing its favorable effect in uveitis on its anti-toxoplasmic basis. The results in these cases of uveitis also indicated that those with a positive dye test as well as a positive complement-fixation test responded better to Daraprim therapy than those in which only the dye test had been positive. Diagnostically, this may be further evidence that when both tests are positive one may be dealing with toxoplasmic etiology. Nevertheless, the evidence would also suggest that a complement-fixation test is not necessary for the diagnosis and that a low titer may be just as indicative of the disease as a high titer. In the cases that responded, the most characteristic lesion seen was a focal chorioretinitis with an associated marked vitreous haze. Usually the most recent lesion was adjacent to an old, healed patch of chorioretinitis.

These authors stress properly the necessity of watching for the toxic effect of Daraprim on the erythropoiesis. They noticed a depression of the blood picture in approximately one third of the cases when 25 mg. of Daraprim was administered daily. The anemia was of the macrocytic normochromic type, and three of their cases showed a neutropenia.

These studies are a stimulus for a therapeutic trial with Daraprim in uveitis. It is essential, if an ophthalmologist does this, that he watch the blood picture carefully. It is most unfortunate that toxoplasma levels, dye-titer and complement-fixation studies are not readily available to all practicing ophthalmologists in the country nor are all ophthalmologists near the few large centers where these studies are available. If Daraprim is used as a therapeutic trial by ophthalmologists on all stubborn cases of uveitis, many people will be subjected needlessly to the toxic potentialities of Daraprim. If many of these individuals were found to have negative dye titers and complement-fixation tests, they would not be tried on this agent.

All the patients in this group received mydriatics and cortisone in addition to the Daraprim tablets. Apparently cortisone did not block the therapeutic activity of Daraprim. There was no mention made in this report of the number of recurrences after cessation of therapy. It will be extremely important to know whether recurrences are more frequent in the apparently successfully treated cases than in those cases of similar clinical appearance with positive dye tests and complement-fixation tests which were not treated with Daraprim. Also, it might be important to know whether the patients would have done as well or better without the steroid in their therapeutic regimen.

Although the authors state that the patient was seen at the end of two weeks and if no untoward reactions were noted, the treatment was continued for another two weeks, they failed to state just how long this routine was prolonged. Before undiagnosed uveitis, posterior uveitis with focal chorioretinitis, and marked vitreous haze are treated indiscriminately with Daraprim, one must determine the length of time the treatment should be continued in order to prevent recurrences and whether or not treatment should be reduced gradually.

IRVING H. LEOPOLD

VASCULAR CHANGES AND CLINICAL RESULTS OBTAINED WITH THE SOLUTION OF BENZYL CINNAMATE WITH VITAMIN A IN ARTERIOSCLEROTIC LESIONS

A PRELIMINARY REPORT

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New York, New York

Am. J. Surg., 1956, *92:* 370–373

The vascular changes resulting from the injection of a solution of benzyl cinnamate and vitamin A have been studied by direct ophthalmoscopic observation in arteriosclerotic lesions of the retina. These changes are characterized by (1) the formation of new vessels, (2) changes in the condition of the arteries, and (3) changes in the condition of the veins.

The formation of new vessels, which has been observed in the cornea and the conjunctiva, as well as in Shrapnell's membrane in patients with chronic con-

ductive deafness, during treatment with benzyl cinnamate solution with vitamin A does not result from strangulation of the vessels by newly formed connective tissue, as in proliferating retinitis or cirrhosis of the liver, nor are the newly formed vessels the result of compression of the vessels by a tumor or by an enlarged gland. Rather, they are the result of proliferation of the capillaries at the site of a lesion, such as that seen during wound healing.

The changes in the arteries are evidenced by better filling, with greater translucency and clearer definition of the blood stream; in addition, the narrowing of the arteries is decreased. The arterioles can be traced farther out to the periphery. The sheathing of the vessels diminishes and it is possible to observe gradual separation of an artery from a vein, both of which coalesced before. As the lumen of the arterioles increases, they are enabled to carry a greater volume of blood so that their hydrostatic pressure becomes correspondingly greater, the outward driving force is increased, and the passage of nutritive substances from the blood to the tissue is greatly facilitated.

A similar increase in translucency appears in the venous blood stream and the tortuosities and dilation of the venules are reduced. The resulting decrease in hydrostatic pressure increases the inward driving force, favoring the passage of the waste substances from the tissue into the blood. At the same time, the diminution in the quantity of blood in the veins increase the venous return and so makes it possible for more blood to circulate in the arteries.

The first clinical results obtained by the use of this solution in the treatment of arteriosclerotic lesions of the retina and of the lower extremities are encouraging. Further experimentation will be needed before the exact effects of the preparation can be evaluated, but the trials already completed have established the following facts:

(1) In a series of 33 patients with arteriosclerotic and diabetic retinopathy who were treated with this preparation, 25 experienced improvement of vision in varying degrees. These were patients who had not been improved by previous methods of therapy and whose vision was gradually diminishing. The degree of improvement depends on the condition of the nerve. When its integrity has been destroyed, no improvement can be expected, but when vision is impaired because there is a lack of blood supply to the nerve, as in arteriosclerosis, or when the perceptive power of the nerve endings is reduced by an inflammatory condition, improvement can be obtained by the use of the preparation.

(2) In a series of 15 patients who were suffering from severe peripheral circulatory insufficiency as a result of obliterative arteriosclerosis, 14 were improved after injections of the benzyl cinnamate solution. Previous treatment had proved ineffective. Improvement in the blood supply to the legs, which which could be seen in the aortograms, was followed by improvement in pain, cramps, and difficulty in walking—symptoms essentially due to an inadequate blood supply.

Comment: Diabetic retinopathy is a worrisome and insomnia-producing disease for all ophthalmologists. Naturally they are quite interested in any measure which offers a

shred of hope to patients with this condition. Therefore, ophthalmologists will grasp at any straw which might afford such patients hope of improvement. Dr. Jacobson's report on the use of benzyl cinnamate with vitamin A in arteriosclerotic lesions suggests that this agent may be of value in diabetic retinopathy. He has reported earlier on some of the vascular action of benzyl cinnamate in the N. Y. State Journal of Medicine, 1953, *53:* 970, and Bulletin Soc. d'Ophth. de Paris, 1936, *48:* 775. He believes that the use of this agent will lead to the formation of new vessels in the retina, alter the pathologic changes of the arteries and produce an increase of vascularization of corneal opacities. Dr. Jacobson has stated that various degrees of improvement in vision have occurred in 25 of 33 cases with arteriosclerotic and diabetic retinopathy treated with this agent. Unfortunately the details of these cases are not presented. This could prove to be an effective agent, but the data presented is totally inadequate to do more than suggest that controlled studies need to be performed with this agent.

IRVING H. LEOPOLD

COMBINATION THERAPY OF RETINOBLASTOMA WITH TRIETHYLENE MELAMINE AND RADIOTHERAPY

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J. A. M. A., 1956, *162:* 1368–1373

Since 1953, the departments of ophthalmology, radiotherapy, and medicine of the Columbia-Presbyterian Medical Center have been engaged in a joint attempt to evaluate the possible additive or synergistic effect of nitrogen mustard analogues and radiotherapy on patients with retinoblastoma. The combined treatment has been given to 55 patients, in 50 of whom it was completed from 6 months to 3 years ago. The patients selected were those in whom adequate preliminary study, consisting of chest, skull, and orbital x-rays and a skeletal x-ray survey; urinalysis; and a complete blood cell and platelet count, in addition to a careful history and physical examination, disclosed that the disease had not extended beyond the local area. The children were generally from 6 months to 2 years of age, with the range being from 2 months to 7 years. Triethylene melamine was used at first, because it was available in a form that could be given orally. This form was later discarded, however, because it was found that emesis and irregularity of absorption interfered with accuracy of dosage, especially when leukopenia or thrombopenia did not develop. Currently, a new preparation of triethylene melamine for parenteral administration is being used. Eight patients have been treated with intramuscular injections and nine with intra-arterial injections made directly into the internal carotid artery.

With repeated examinations by an experienced ophthalmologist, the eventual

outcome of therapy for retinoblastoma is generally predictable in less than 5 years after completion of treatment, because of calcification and certain other characteristics accompanying its arrest. A review of the results obtained with the orally administered triethylene melamine and radiotherapy in the first 33 children treated shows that the tumor was arrested and useful vision preserved in 12, or 36 per cent. All patients were treated, no matter how large the lesion, if it was felt that some vision could be preserved. The best results, however, were obtained in patients with small or medium-sized tumors. Nine of the 11 patients in this category showed a favorable response, whereas only 2 of a group of 10 children with large tumors responded favorably to the combination therapy.

At present, 7 of the 8 children to whom triethylene melamine has been given intramuscularly have tumor arrest with retention of useful vision and one is alive with tumor arrest but no vision. A moderate leukopenic or thrombopenic effect, or both, was obtained in almost all the patients treated intramuscularly, whereas there were many instances in which mild or no marrow depression was observed after oral administration of triethylene melamine. The possibility that larger doses were responsible for better results in the intramuscularly treated group is under study.

The intra-arterial method was used (1) when the tumor was found to be very large but enucleation was refused by the parents, (2) when tumor cells were seen histologically at the cut end of the optic nerve at the time of enucleation (formerly an invariably fatal situation), or (3) when an orbital regrowth of tumor was present after an earlier enucleation. In addition to triethyelene melamine therapy, radiotherapy was given to the eye or orbit, and if necessary orbital exenteration was performed. Two of these "almost hopeless" patients have had the tumor arrested and vision preserved, three have died, and the other four apparently have active disease. Before 1953, no attempt would have been made to treat these children.

One child in the series of 50 patients, many of whom had received from four to six treatments with triethylene melamine, died of effects directly related to marrow depression. This child suffered a head injury while thrombopenia was present and later died at another hospital of a subdural hematoma. In this patient leukopenia had appeared after only two days, a serious prognostic sign in the experience under review. When leukopenia did not occur before the fifth day, marked depression was rarely seen. Since this episode early in the study, the children have been given prednisone (Meticorten) and a broad-spectrum antibiotic in an empirical attempt to prevent bleeding manifestations and infection if the platelet count fell below 50,000 per cu. mm. and/or the white blood cell count fell below 2,000 per cu. mm. Prednisone was given orally in a dose of 2.5 mg. four times a day until the platelet count returned to 100,000, after which it was gradually discontinued, and the antibiotic was given until the leukocyte count returned to 3,000. In only one instance in the entire series was a transfusion required. The marrow depression that may occur after triethylene melamine therapy is often a useful indicator of adequate dosage. Com-

plete blood cell counts with platelet counts were performed two or three times weekly after treatment. Additional safety is provided by the platelet counts, because their return to normal is later than that of the leukocyte count. Consequently, further treatment was withheld after the platelet depression reached its low point (100,000 or below) until the platelets rose above 200,000 per cu. mm. and the leukocytes above 6,000. Nausea and vomiting occurred in about one-half of the children treated, but was either mild or easily controlled with chlorpromazine. Temperatures as high as 101°F. (38.3°C.) were noted in a few of the smaller children during the first 24 hours.

If the 9 patients who received intra-arterial chemotherapy in an attempt to control an otherwise hopeless situation are excluded, then 19, or 46 per cent, of 41 patients have exhibited apparent arrest of the tumor. The results achieved with combination therapy of patients with either small or medium-sized tumors indicate that arrest has apparently been secured in 12 of 14, or 85 per cent; in addition, useful vision has been retained. Future results may be still better in the children given triethylene melamine intramuscularly, since the small group of patients so treated up to the present time has shown the highest percentage of arrested tumors.

The total dose employed has been empirical, with an average course of 15 mg. orally or from 6 to 10 mg. intramuscularly extended over a period of from 6 to 12 months. These young children apparently tolerate much larger doses than do adults, since the recommended parenteral dose of triethylene melamine in adults is only from 6 to 12 mg.

If it is true, as various investigations have indicated, that radiotherapy and chemotherapy exert their effect at different points on the chromosome of the dividing nucleus, then the action of these agents may quite possibly be synergistic.

Comment: One can not help but be impressed with the results following the use of a combination of radiotherapy and triethylene melamine in 50 children so treated for retinoblastomas. The results definitely indicate a superiority of this form of therapy over the use of radiation alone, as studied in a previous series. Outstanding features in this study are the number of cases and the great pains which have been taken to control the observations and the conclusions. The potential value of chemotherapy in ocular tumors creates many new problems.

This study has already shown that the optimal intramuscular dose is 0.1 mg./kg. However, the variation in individual sensitivity demands that subsequent therapy in each patient be based on initial hematological response. The total dose employed has averaged approximately 6 to 10 mg. intramuscularly extended over a 6 to 12 month period. The youngsters appeared to be able to tolerate this drug better in larger doses than adults.

This is an encouraging note in the therapy of a previously discouraging disease. The results of future studies in this large center where these cases are concentrated should be watched with exceeding interest by all ophthalmologists.

IRVING H. LEOPOLD

RADIOTHERAPY IN OPHTHALMOLOGY

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Ophthalmologic conditions can not be properly treated by radiotherapy without a thorough understanding of the harmful sequelae that may follow its use.

Grenz ray radiation (half value layer 0.04 mm. aluminum) may produce increased pigmentation of the skin. For this reason treatment to the lids should be avoided. With doses over 5,000 r in air the only complication observed has been telangiectasis of the conjunctiva.

Beta radiation with doses ranging from 2,300 to 32,000 rep (roentgen equivalent physical) on the surface has been observed to produce telangiectasis and keratinization of the conjunctiva, atrophy of the sclera, punctate keratitis, corneal vascularization and scarring, iritis, iris atrophy, and radiation cataract.

The harmful effects observed with the more penetrating ionizing rays of various qualities are atrophy, depigmentation, increased pigmentation and telangiectasis of the skin, atrophy of the tarsal plate, epilation of lashes, atrophy and fibrosis of the sub-epithelial tissues, keratinization of the conjunctival epithelium, atrophy and telangiectasis of the conjunctiva, and atrophy of the sclera with occasional perforation. The cornea may develop punctate keratitis, edema, keratinization, scarring, thinning with or without perforation, and vascularization. Other effects are iritis, iris atrophy, atrophic degeneration of the ciliary body, and radiation cataract. Retinal changes include vascular occlusion; new vessel formation; sheathing; hard, white deposits (edema residues); edema; retinal, preretinal, and vitreous hemorrhages; retinitis proliferans; retinal detachment; and secondary glaucoma. In children, irradiation of growing bone may arrest its development.

Superficial therapy may be given with either Grenz rays or beta radiation, since the effect on the tissues is essentially the same whichever is used. Most of the lesions treated with superficial therapy are benign and the doses should therefore be conservative. Conditions treated by superficial therapy include vernal catarrh, corneal vascularization, precancerous melanosis of the cornea and conjunctiva, recurrent pterygia, nodular episcleritis, phlyctenular keratitis, bullous and filamentary keratitis, and resistant corneal ulcers. A total dose of from 3,000 to 5,000 r in air or rep on the surface in three to five weeks is suggested for vernal catarrh. In 90 per cent of the cases, however, this is a self-limiting disease and other local measures are usually equally effective. Radiotherapy with conservative doses has produced extremely variable results in patients with corneal vascularization. In many cases the corneal vessels may

regress spontaneously once the irritation is removed, and local measures should therefore be fully tried before radiation is undertaken. Radiation before keratoplasty may result in non-union of the graft. The diagnosis in precancerous melanosis must be established by biopsy, after which a satisfactory response can usually be obtained by a total dose of from 3,000 to 5,000 r in air or rep on the surface in from two to four weeks. In recurrent pterygia, therapy should be started the first or second day after excision of the lesions. Small, early recurrences, however, may be treated without further surgery. Nodular episcleritis requires radiation only in cases resistant to other forms of treatment. Diffuse episcleritis has been refractory to radiotherapy. Similarly, radiation treatment is recommended for phlyctenular keratitis only when other measures have failed. The treatment of bullous and filamentary keratitis is designed to utilize the analgesic effect of Grenz rays on the cornea, but no change in its appearance should be expected. The beneficial effect of radiation on corneal ulcers is likewise believed to be due to its analgesic action. Conditions in which radiation has not been found necessary include anterior ocular tuberculosis, papillomas, granulomas and small hemangiomas.

Harder, more penetrating x-rays (low voltage therapy, with kilovoltages ranging from 60 to 120 kv.) may be used to good effect in treating epithelization of the anterior chamber and basal-cell and squamous-cell carcinomas of the lids. In patients with epithelization of the anterior chamber, the down-growing epithelium should be observed to be certain it is progressing, since it sometimes stops or even regresses spontaneously. When corneal edema is present, the prognosis must be guarded. A total dose of 5,000 r should not be exceeded, because higher doses may lead to corneal edema. Epithelial cysts respond poorly to irradiation and are better treated by diathermy.

The survivals and cosmetic results obtained with radiation in patients with carcinoma of the lids (either basal-cell or squamous-cell) equal those obtained with surgery and the choice of treatment must be made according to the requirements in each case. In general, the older the patient and the larger the lesion, the more radiation is to be preferred. Adequate shielding of the globe is essential.

High-voltage therapy is indicated in retinoblastoma, lymphosarcoma, hemangioma, and metastatic carcinoma to the choroid or orbit. Retinoblastoma is treated by irradiation only when it is bilateral. The more severely affected eye is enucleated and the fellow eye is treated. When lymphosarcoma is confined to the eye or the orbit and the disease does not become generalized within five years, the prognosis is good. The disease involves primarily the orbit, but it may also affect the lids, conjunctiva, lacrimal sac, or lacrimal gland. Protection of the uninvolved structures is essential and is accomplished by special shielding.

Irradiation may be beneficial in the treatment of large cavernous hemangiomas of the orbit and lids, either alone or in association with sclerosing solutions and carbon dioxide snow. The doses should be minimal and the eye must be shielded. In patients with metastatic carcinoma for whom treatment is in-

dicated, palliation can be secured and useful vision maintained in about half the cases.

Eale's disease and diabetic retinopathy have not responded satisfactorily to radiotherapy in the author's experience, and treatment is not recommended.

Comment: Dr. Merriam's paper is of great value because it stresses the harmful effects of the injudicious use of radiotherapy. He has touched on the potential dangers of beta rays. Although they do not penetrate deeply, they may penetrate sufficiently to damage the periphery of the lens so that cataracts may develop many years after exposure of the eye to this type of radiation.

The results as reported by Dr. Merriam are not persuasive for the use of radiotherapy in the treatment of corneal ulcers, recurrent pterygia, phlectenular keratoconjunctivitis, or in vernal catarrh. He feels that in the latter disease irradiation should not be used as a primary procedure. It is important to note that before keratoplasty irradiation may predispose to the non-union of a graft.

The chief value of irradiation would appear to lie in malignant disease of the lids and of the globe, but here also radiotherapy is not recommended unless the diagnosis has been confirmed by histology.

It is important to realize that radiotherapy may be of help in some extremely resistant ocular diseases which fail to respond to any other therapy. One should never employ this therapy without full realization of all of the undesirable side and latent effects.

IRVING H. LEOPOLD

INJURIES

FORTY-SEVEN CONSECUTIVE CASES OF INTRAOCULAR FOREIGN BODY

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The prognosis in cases of retained intraocular foreign body is discussed in the light of the experience gained in a consecutive series of 47 such cases, occurring over a 20-month period, which were dealt with almost exclusively by the anterior route method of extraction using an immobile giant magnet. Variable factors, such as the size of the foreign body and the depth of penetration, have of course been taken into account. Most of the patients, who had an average age of 34 years, were working men and it is significant that in 24 cases (51 per cent) the injuries were caused by one particular type of maneuver, that of striking the head of a chisel or some other metal tool with a hand hammer; in another 6 they were caused by metal chippings flying from a neighboring workman's hammering. With the exception of certain of the hammer and chisel accidents the industrial injuries in this series occurred in spite of normal personal protective measures and in circumstances which were for the most part unforeseeable.

Most of the patients (31) attended within 5 hours of injury and had the foreign body extracted within 24 hours; 4 were seen the day after the injury; and 5 others within 8 days. The remaining seven patients attended after considerably longer intervals. Most of the 16 patients who had delayed had been aware of an eye injury but had ignored it as trivial until the onset of symptoms. None of the late-comers complained of pain, only that the eye was red or sore or that vision was deteriorating. This lack of pain contrasted strongly with the distress caused by a superficial corneal or subtarsal foreign body which sends the patient hurrying to the casualty department. Irritation of the tissues was seen infrequently because of the promptness with which the foreign body was extracted in most cases.

The question of infection is important in considering the effect of delay in removing a foreign body on the ultimate prognosis. Speed of extraction is still essential, because, although antibiotics can be used as a prophylaxis against infection, they are not always effective and intraocular infection, once established, is hard to control so that useful vision is retained.

All but seven of the retained foreign bodies were capable of being magnetized. The non-magnetic foreign bodies consisted of two 2.5-cm. lengths of copper wire, a minute metal particle, a brass chipping, two small (less than 1 c. mm. radiologically) unrecovered particles, and an airgun pellet. Neither of the cop-

per wires penetrated further than the cornea but both had come to rest in the anterior chamber from which they were removed with difficulty. The unrecovered particles had been *in situ* for 2½ years and 78 days respectively and since vision was good and there were no degenerative changes in the eyes, it was decided to leave them undisturbed.

The excision rate for this series is 12.8 per cent (six cases, four magnetic and two non-magnetic). The size of the foreign body concerned averaged 90 c. mm. Three of these eyes were lost because of infection—one because of an intractable cyclitis, and two because of irreparable damage to the eye by foreign bodies of about 250 c. mm. each. Intraocular infection occurred in four cases, two before and two after operation, and all but one patient lost the eye. In this one patient intensive chemotherapy controlled the infection, but he was the only one in the series in whom an established intraocular infection could be controlled and the eye retained.

It has been argued that the anterior route method of extraction, which was used in all but three of these cases, is suitable only for small foreign bodies. Experience in this series, however, has shown that the larger foreign bodies are also readily accessible by the anterior route. The larger particles that are rectangular in shape present end-on to the magnet and slide forward easily without further damage to the intraocular tissues. Irregularly shaped foreign bodies cause large entry wounds and extensive damage to the unresisting intraocular tissues. These wounds require surgical repair and it is felt to be better surgical practice to withdraw the foreign body along its track of entry and out through the entry wound, rather than to create a second track towards a second incisional wound in the globe, which adds to the trauma and increases the risk of complications. Patients with gaping entry wounds and prolapsed uveal tissue were treated as acute emergencies and were operated on at once, pausing only for x-ray examination. Care was taken in all cases to dilate the pupil fully to facilitate the passage of the foreign body forwards into the anterior chamber and to prevent its becoming entangled in the iris. This procedure made it unnecessary to perform an iridectomy. The keratome section was always made at the temporal side in order to take advantage of the wide approach to the globe in which to maneuver the hand magnet.

The size of the foreign body is an important factor in prognosis. Using the volume of the foreign body as the critical factor, it was found that in 19 cases in which the foreign body had a volume of less than 1 c. mm., 6/9 vision or better was secured. Three more foreign bodies less than 1 c. mm. in volume were responsible for injury to the lens. This was an incidence of 13.6 per cent, as compared with 37.5 per cent for foreign bodies over 1 c. mm. in size. Corneal penetration occurred in only three patients; in seven the foreign body penetrated the cornea and became embedded in the iris. Damage to the lens occurred in 17 patients, 7 of whom had intralental foreign bodies while in the other 10 the foreign body passed through the lens. From the point of view of visual result, only 4 of the 17 patients with lens involvement achieved vision of 6/6 with stationary opacities. The remainder either had complete opacifica-

tion (6 cases) or became aphakic (7 cases). Patients in the second group all had a prolonged convalescence because the flocculating lens cortex herniated into the anterior chamber, causing non-infective post-traumatic uveitis which resolved as the cortex absorbed.

Penetration to the vitreous either through the iris and zonule (9 cases) or through the sclera (9 cases) occurred in 18 patients. A higher proportion of these achieved good vision of 6/9 or better (50 per cent) than of those in whom the lens was damaged during the passage of the foreign body into the posterior segment (30 per cent).

Blind magnet trials should not be used to prove the presence of a foreign body, because they are certain to increase intraocular damage and make worse the prognosis.

A disadvantage of the anterior route method is the fact that the patient is unable to cooperate fully. If the giant magnet is to be used, the patient should be able to gaze steadily in the required direction while it is applied to the eye. A ciliary ganglion block, which destroys the ability to cooperate by inducing third nerve paresis, is of no help until after the foreign body has come forward into the anterior chamber. Adequate surface anesthesia, however, is essential.

Comment: This is a report of 47 intraocular metallic foreign bodies observed in civil practice at the Manchester Royal Eye Hospital. The most interesting group consists of the cases in which the objects had penetrated the lens and entered the vitreous. My personal experience does not substantiate the author's emphasis upon the virtues of the anterior route in these cases. Invariably, vitreous will be lost when the foreign body is brought around or through the lens and an extremely stormy postoperative recovery occurs. After a personal experience of this sort in several cases, I learned, as did many other eye surgeons, that it was much better to remove the foreign body through a posterior approach, thus permitting the lens capsule to seal over and shut off the vitreous. It was later possible to remove such lens substance as did not become absorbed. This technique has proved equally successful in post-war civilian practice.

GEORGE M. HAIK

SURGICAL REPAIR OF CORNEAL INJURY

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California Med., 1956, *85:* 320–325

A careful, complete history, including exactly what the patient was doing at the time of the injury, is required in all cases of corneal injury. The first aid and any later treatment should then be evaluated, because it is important to know whether anything was removed from the eye and whether there are in-

dications of a deep or penetrating injury or the presence of an intraocular foreign body. The history alone often suggests the need for an x-ray examination.

In examining the patient, the vision of each eye must be separately determined and recorded before any fluid is instilled or anything removed. If the injuries are painful, the lids will have to be held open while the vision is determined. After this has been done, the examination should be completed in minute detail. Deep, non-penetrating wounds of the cornea are either tangential or flap. If the examination has been delayed, little can be done with a flap wound except to excise the flap, because the tissue will already have become necrotic. In early cases, however, much can and should be done. Usually the injuries are extensive and the pupillary area is involved. After debridement and irrigation with saline solution, the extent of the damage and the length of the wound are determined with the spatula and the suturing is begun. The sutures must be placed with extreme care and exactness, starting in the flap and ending in normal corneal tissue. If a suture is not well placed, it should be removed without hesitation. If difficulty is encountered in determining whether a wound extends all the way through the cornea, a drop of fluorescein may be put in the conjunctival sac. If the wound is penetrating, a green color will appear at once in the anterior chamber as viewed under the slit lamp.

All leaking wounds, open or perpendicular to the surface of the cornea, or both, are dangerous and should be closed promptly. The lids have a milking action which results in a loss of aqueous fluid and the entrance of conjunctival fluid into the anterior chamber which may be followed rapidly by severe infection. No two penetrating wounds of the cornea are alike. Penetrating wounds of the center are generally leaking, perpendicular wounds complicated by lens damage. Such wounds always heal more slowly than those about the periphery because of the lesser nutrition of the central cornea and they are usually accompanied by considerable visual loss.

For corneal suturing it is essential to have magnification (such as that obtained with the Zeiss telescopic loupe), instruments that are in good repair, and fine, sharp needles and thin, strong braided silk. Anesthesia must be deep, either local or general, and in either a retrobulbar injection of procaine with epinephrine is recommended. In general, one corneal suture should be put in for every two or three millimeters of wound length. The sutures are placed before any of the complications are dealt with. In a jagged or angular wound one or more single sutures at the apex of the "V" will be needed and the closure may be extremely difficult.

After the sutures have been placed, attention is given to the complications. In small wounds in which the iris is caught or has adhered to the inner surface of the cornea, it can usually be freed by irrigation or stroked loose with an iris spatula. A few drops of sterile epinephrine in an eye with an open wound will give rapid, maximal dilatation and may pull the iris free when the pupillary portion is caught in a centrally located laceration. Iris incarceration near the base is freed with the iris spatula and a small peripheral iridectomy is carried

out before the sutures are tied. An air bubble will maintain the depth of the anterior chamber. A prolapsed iris should be replaced or irrigated back to its normal position if the wound is recent, if the prolapse is small, or if it has occurred during the placement of the sutures. In old wounds, however, the iris may never be replaced but must be excised. If the corneal laceration is extensive with vitreous or lens material in the wound, the sutures should be preplaced and then all the prolapsed material should be removed (lens material before the sutures are tied and vitreous afterwards). In cases of lens or vitreous prolapse a wide iridectomy is performed. When the lens capsule is opened widely, a cataract extraction is usually necessary in the next few days. If lens material, especially capsule, is allowed to heal in a corneal wound, a fistulous tract usually develops and epithelial downgrowth is likely to occur. Vitreous in the wound means that there is vitreous in the anterior chamber, with the possibility of secondary glaucoma. Lens dislocation, partial or complete, may be a complication, and bullous keratitis is often a late result.

Conjunctival flaps alone should not be used to cover corneal wounds. If the eye is so severely damaged that a conjunctival flap is the only procedure available, enucleation is probably the best operation in most cases. Sometimes, if only a small piece of corneal tissue is missing, the wound can be made linear and then sutured. Painful corneal scars, cystoid cicatrices, corneal fistula, and old iris prolapse at the limbus may require excision. Resection of corneal scars without grafting is rarely done because lamellar keratoplasty is only slightly more difficult and excellent results are obtained much more often.

Superficial foreign bodies are all removed and curettement carried out under a slit lamp with deep cocaine anesthesia. An infection in a penetrating wound of the cornea is usually primary in the wound itself and it is usually best to delay operation for 24 or 48 hours—time for antibiotics given at the time of injury to control the infection. If it is not controlled promptly, the advantages of closure must be weighed against the probability that the infection will become exacerbated. Ring abscesses of the cornea may occur within 24 hours, and infection due to *P. pyocyaneus* is rarely stopped. Except for these two conditions, antibiotic therapy is usually effective and the operation can be successfully performed.

ECONOMICS, SOCIAL AND LEGISLATIVE

OCCUPATIONAL THERAPY FOR BLIND PATIENTS

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Occupational therapy for the blinded patient must be considered in a specialized category just as much as that for the amputee or the paraplegic. The realization of the experiences through which the patient is passing in any major deprivation requires a temperamental aptitude for dealing with the difficulties inherent in such a situation. As a result, the educational background of the qualified occupational therapist is particularly important. In addition, certain basic standards that have been developed in relation to blindness should be constantly reviewed and studied.

There is only one factor that is common to all blind people, and that is the practical difficulty of not being able to see. This is both a great impediment to all kinds of action and psychologically a reality of the negative kind that tends to drown out awareness of other realities in the patient's life. Individual motivation should be considered in planning the therapeutic activity of any blind person because there are almost as many different reactions to blindness as there are blind persons. The classic concept of "arts and crafts" for the blind has gradually given way to a realization of the fact that the chief requirement in planning activities for the blind is a constant effort to adapt ever new activities to performance without sight. This phase of a therapist's work is by no means easy. Since it is essential for the therapist to remain aware of the realities of the situation, blindfolding, though sometimes criticized by the blind themselves, must be considered an indispensable part of the necessary training. Ability to function with the sight cut off, however, should not be used to build up any prestige with the patient, but should be used only as a learning device by which a better understanding of certain physical handicaps of the blind can be obtained.

The therapist can profit by studying the various classic ways of doing things without sight in order to become familiar with the methods and short cuts that others have devised, but her constant effort should be to put herself in the blind person's position, using all her ingenuity to overcome the difficulties it presents. It must be remembered that work with the blind requires greater patience than work with other handicapped persons, not because blind patients are difficult as a group, but because blindness as a living condition is excessively frustrating, and this frustration often passes over to the seeing persons associated with blind

ones. A serious hazard to a blind rehabilitation program is a tendency to underestimate the manner in which the feelings of sighted workers can complicate the entire problem. Simple denial of the existence of these feelings is wholly futile, tending to dam them up and often leading to disguised hostility toward the blind. The therapist should always have interests apart from social problems and blindness from which to draw not only a new and refreshing point of view but also material with which to enrich the experience of the blind people with whom she works, and for whom she is the source of a large amount of information. In this connection, it may be observed that the reputed suspiciousness of the blind is often attributable to the unreliability of the information they receive. Great care and accuracy of observation should be used in collecting and reporting information to the blind, because inaccuracy may lead to serious consequences when the listener is unable to verify the facts with his own eyes.

All blind patients, whether psychotic or not, fumble more than most beginners, and this obliges the therapist to spend time waiting. When rightly used, these waiting periods provide her with an opportunity to add to her knowledge and skills as a worker with the blind. The patient should be kept aware of the therapist's interest, which must be audibly expressed from time to time; too much conversation, however, merely distracts the patient's attention and should be avoided.

The supposition that blind people "sense" facts by mysterious means should be discounted. As a rule, they obtain their information by perfectly logical methods, such as learning to interpret the tone of the voice, upon which they rely far more than do those who can see the facial expressions of their interlocutors. The seeing person, too, should develop special techniques for determining how the blind person is reacting. Since the expression of the blind person's eye is of no help, the therapist should watch his mouth, if it is an expressive one, and should also note the tension or relaxation of the hands and feet which often indicate his reactions. Most of all, she should lead the blind person to express himself in words, without boring him or giving him the impression that his affairs and feelings are being probed.

These observations apply chiefly to normal blind persons. Added psychiatric difficulties and limitations complicate the problem still further. Therapeutic programs for seriously regressed blind patients are all in the experimental stage at the present time.

Common sense should be used in meeting the problems of the blind and the progress made should be carefully recorded. A decade of good clinical notes on occupational therapy with the blind would be of great assistance in acquiring an understanding of blindness.

Comment: The obligations of an ophthalmologist to his patient should not cease if the patient loses his vision; rather they should become even greater. Obviously it is impossible for the doctor to himself instruct the patient since he has neither the time nor knowledge of the techniques used by experts in this field, but it is of extreme impor-

tance that he know competent people to whom to refer the patient and that he stand ready at all times to lend moral and psychologic support if it is needed. Such competent people should above all be able to adjust themselves to properly deal with the newly blinded; they should not be so rigid that they cannot readily adopt new techniques for individual patients as might seem necessary. In small communities, such expert help may not be available, but if the patient is to become a well adjusted person who can live up to his full potentialities, this help should be sought.

DANIEL SNYDACKER

Basic Sciences

ANATOMY

BLOOD VESSELS OF THE BULBAR CONJUNCTIVA IN MAN

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The making of an adequate survey of the capillary bed for study of the variations in its functional activity requires tissue in which the vessels can be traced from the arteriolar to the venular ends, and in which, at the same time, they can be exposed for observation with a minimum of trauma, so as not to upset the normal activity of the functioning components of the bed. In man, the only available site that fulfills these requirements is the bulbar conjunctiva. Most of the studies hitherto made of the topography of the minute vessels have been carried out in animals, and it was not possible to assume that the same vascular phenomena occurred in man. Two series of normal healthy subjects were therefore examined in an attempt to determine the normal appearances of the minute vessels of the bulbar conjunctiva in man, and to find out whether or not there existed a structural or a functional pattern of architecture.

The first series consisted of 60 subjects (36 male) aged between 9 and 76 years, in each of whom the left lateral bulbar conjunctiva was examined thoroughly on one occasion. The purpose of this study was to acquire familiarity with the normal appearances of the conjunctival blood vessels and to be able to differentiate the various vascular elements. The second series consisted of 8 normal, healthy young subjects (3 male), aged between 23 and 31 years. In this group, one area of bulbar conjunctiva was examined repeatedly over a period of not less than two months. Each subject examined felt well and gave no history of previous eye disease, and in each the blood pressure was within the normal range for age.

The subject, who was seated for examination at an ophthalmological slit-lamp table, had his gaze directed laterally to an object so placed as to expose the maximum area of lateral bulbar conjunctiva compatible with comfort. The exposed area was observed directly through a stereoscopic dissecting microscope, using paired ×5 or ×10 objective glasses and paired ×10 eyepieces. This optical system therefore gave magnifications of 50 or 100 diameters. A piece of heat-resisting glass was introduced between the light-source and the conjunctiva in order to eliminate the effects of temperature changes on the minute blood vessels.

In the second part of the investigation, an arteriole was selected at random at the initial examination and the region of distribution of its branches was noted. Several photomicrographs were then obtained, each focused at a slightly different point within the area to be studied. The sharply focused areas from the various prints so obtained were then cut out and pieced together to form a composite photomicrograph which formed the basic plan for all future observations. Upon it were marked the direction of blood flow and the appearance of any blood vessels not apparent at the time of photography. When, after repeated observations, it seemed probable that all blood vessels normally open had been observed, adrenaline hydrochloride (1:1,000) was instilled into the conjunctival sac and the behavior of each blood vessel was noted. Later, the minimum concentration of adrenaline required to produce a discernible change in the blood vessels (the adrenaline threshold) was determined. In these subjects, it ranged from 1:5,000 to 1:25,000.

Three groups of blood vessels can be recognized: the posterior conjunctival vessels, or conjunctival vessels proper; the anterior conjunctival vessels; and the anterior ciliary vessels. Another type of vessel, the aqueous vein, is also found in the conjunctiva. These vessels emerge from the deeper ocular structures some 2 mm. from the limbus and run centrifugally. They are filled partly with a clear fluid and partly with blood, and are believed to be exit channels for the aqueous.

Detailed examinations were made only of the posterior conjunctival vessels. All types of minute vessel could be recognized. It was possible to identify arterioles, capillaries, and venules, both by their appearance and by the direction of blood flow within them. The walls of the blood vessels were not normally visible but the width of the stream of circulating blood, in the absence of anemia and hemodilution, provided a fairly accurate indication of the diameter of the vessel.

The most striking feature of the minute vessels of the bulbar conjunctiva was the existence of many arteriovenous communications, frequently tortuous, uneven in caliber, and much wider in diameter than the capillaries. These vessels were always open, even after the local application of adrenaline. Each arteriovenous communication gave off capillary branches in its proximal portion and received similar branches in its distal segment. There was often a considerable length of vessel in between which neither gave off nor received branches. This disposition of the capillaries around a central arteriovenous communication was similar to that described by Chambers and Zweifach in the mesentery of animals, although the central channel in the conjunctiva was wider. Functionally, the communications provided a mechanism by which rather large quantities of blood could be delivered into the veins when the capillaries themselves were closed. By their behavior, they resembled thoroughfare channels, a conclusion in accord with the findings of Grafflin and Corddry.

The observations of the bulbar conjunctiva in man, made in this study, indicate that a structural pattern of architecture of the minute vessels does exist, but in a limited degree, and that it is certainly not so complete as that described in the mesentery of animals. No true arteriovenous anastomoses were

seen. The demonstration of arteriovenous communications of diameter considerably larger than that of the capillaries but not properly called arteriovenous anastomoses casts doubt on the validity of experiments in which glass spheres have been used to show the existence of vascular shunts. It is, of course, essential to define the term arteriovenous anastomosis. Typically, such an anastomosis is a short muscular vessel that serves to shunt blood from an artery to the corresponding vein, and the term arteriovenous anastomosis should not be applied indiscriminately to any dilated channel joining an artery to a vein.

Comment: This study of the vascular pattern in the conjunctiva of "normal" human subjects is interesting and complete. The article should stimulate further study of normal human subjects in order to provide a firm basis for the reports concerning pathologic changes in conjunctival vessels. The marked difference in the vascular patterns of the eight subjects is significant because it indicates the caution required in considering abnormalities in persons with vascular or conjunctival disease. Despite the variation in the individual subjects there does appear to be a general pattern of circulation from the arterial to the venous side that makes possible two principal channels for blood flow (through the capillary head or thoroughfare channels).

ALBERT N. LEMOINE, JR

BIOCHEMISTRY

THE PHOSPHORUS METABOLISM IN THE LENS

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Phosphate is of great importance to the metabolism of the cell. In its inorganic form the phosphate ion acts as an electrolyte in the maintenance of osmotic pressure. Since it is a tribasic acid, phosphoric acid is particularly helpful in keeping the hydrogen-ion concentration constant. It also acts as a buffer because it is capable of altering its degree of dissociation. Phosphate is required as a reaction-partner in many fermentation processes. It is also an important basic material of such vitally necessary substances as, for instance, the phosphatides (lecithin, cephalin, sphingomyeline). In addition, it is an essential component of nucleic acids, that is to say, of the chromosomes and genes which are the substances of the nucleus and cell-plasma that are essential to life. The phosphate ion is also important as a component of vitamins and co-ferments.

Phosphate plays a special part in the energy metabolism. It is the task of the phosphate metabolism to collect the energy gained from the catabolism of nutrients in phosphate compounds rich in energy, to store it, to transport it to the points at which it is required, and to make it available at those points.

Since the process of phosphate metabolism is intimately connected with general metabolism, and especially with oxidative metabolism, the localization of the oxidative metabolism process naturally coincides with that of the most active phosphate metabolism. The fact that oxidative metabolism is not distributed uniformly over the lens and that phosphate metabolism is most active where mitochondria occur is explained by the anatomic structure of the lens. The investigative work of various researchers seems to show that phosphate metabolism is most active in the lens epithelium, as might be expected from its very active general oxidative metabolism. The cortical strata are also capable of synthesizing adenosine triphosphate, which is the most important of the energy-rich phosphates, but hardly any of this substance can be shown to occur in the nucleus.

Determinations of the total phosphate content of the lens have been made by several investigators, but the figures so obtained do not provide a basis for significant conclusions concerning metabolic processes. The only basis for a detailed study of phosphate metabolism is the determination of the individual phosphate fractions. Generally speaking, however, studies of the total content seem to show that the phosphate content in the ash of the lens decreases in

senile cataract, tetany cataract, and galactose cataract. A considerable difference in phosphate content has also been found in juvenile, as compared with adult human lenses; variations in intensity of staining suggest that the phosphate content of the different parts of the lens decreases with advancing age.

The three main groups within the total phosphate content are the phospholipoids, the protein phosphates, and the acid-soluble phosphates. The phospholipoids occur in the lens tissue, and also in every cell in the organism. The share of this phosphate compound in the total phosphate in the lens is probably from 15 to 25 per cent. The phospholipoids, which have been said to represent some 60 per cent of the total lipoid content of the lens, consist of lecithins, cephalins, and sphingomyelines. The lecithins alone make up 65 per cent of the phospholipoids. The total content of phosphatides of the bovine lens has been given as 0.65 per cent on a dry weight basis. Whether the other two fractions of the phospholipoids, namely acetyl-phosphatide and the phosphatic acids, occur in the lens does not seem to have been the subject of separate investigation. Relatively little is known of the importance of the phosphatides in the general cell metabolism, but they are known to be necessary for the maintenance of life. The interface activity of these compounds depends on their physicochemical properties. By reason of their polar structure they are capable of forming membranes. The compactness of these membranes depends on the concentration of the phospholipoids. Consequently, they are of importance with regard to the permeability of the cell walls to ions.

It is not yet known whether the phospholipoids can be formed in the lens. We know that, in the case of the other cells, their formation is dependent on oxidative metabolism. This indicates that relatively large quantities of energy are needed for their formation. So far, the presence of the enzymes necessary for this purpose has not been proved. The capacity of splitting up the phospholipoids has been attributed by Salit to the lens affected by cataract. Extensive investigations convinced him that, in the healthy human lens, a slight augmentation of the phospholipoids occurs with increasing age. On the other hand, he found a clear augmentation in lenses affected by cataract as the age of the patients increased. Thus, the phospholipoid content of the lens affected by cataract rose from 0.453 mg. per cent in the fifth decade of life to 0.533 mg. per cent of fresh weight in the ninth decade.

The second main group of phosphate compounds in the cell, the protein phosphates, under which may be classed the phosphoproteids and nucleic acids, has been investigated little, as yet, in the lens.

The phospholipoids of the third group are those that are dissolved in the acid cell extract after the protein has been precipitated. They comprise inorganic phosphate (orthophosphate), the intermediate phosphate esters, the nucleotides—for example, adenyl phosphates and phosphocreatine (phosphagen)—and all of them take part in the catabolism of carbohydrates. The total acid-soluble phosphate in the lens decreases as the subject grows older. Süllmann (1937a) attributed this decrease with age to a diminution in the capacity to form phosphate esters; he does not believe that the lower permeability of the

capsule of the lens of an older subject is responsible. In cases of mature cataract the acid-soluble phosphate fraction may increase sharply, while the organic fraction disappears almost entirely. As much as 200 mg. per cent of inorganic phosphate, calculated on the fresh weight, has been found in cattle cataract, while the organic acid-soluble fraction had disappeared completely. In these cases an infiltration of phosphate must certainly have taken place; infiltration of this kind is probably connected with the calcification of the cataractous lens.

The inorganic phosphate is determined in the acid lens extract by direct analysis. Unless it is determined immediately after the death of the test animal, there may well be an increase in the inorganic phosphate content of the lens as a result of the action of phosphatase (particularly on the unstable phosphagen). In most investigations, especially when animals from slaughterhouses were used, neglect of this precaution must have resulted in the intrusion of error. From studies made in cattle, rabbits, and rats, it seems that the inorganic phosphate content of the lens decreases with advancing age.

The acid-soluble organic phosphate, which represents the difference between the total acid-soluble phosphate and the inorganic phosphate, is composed of a large number of phosphoric acid esters. These esters can be divided into fractions that are difficult to hydrolyze and fractions that are easy to hydrolyze. One of the easily hydrolyzed fractions that plays a special part is the one that is hydrolyzable in 7 minutes. The bulk of this fraction is made up of adenosine triphosphate and glucose-1-phosphate. The figures for the 7-minute hydrolyzable phosphate show that as age advances there is a decrease in the amount of this fraction in the lens. When the amount of the 7-minute hydrolyzable phosphate is subtracted from the acid-soluble organic phosphate, the remaining material is what is known as the "residual phosphate." The figures for this fraction have been determined only on rare occasions. Determination of the 7-minute hydrolyzable phosphate and of the residual phosphate is in reality the determination of phosphate fractions each of which is made up of various phosphoric esters and each of which contains proportions of certain phosphoric esters. This fact must be borne in mind when conclusions are being drawn from the results.

It has been shown by investigations relating to the penetration of phosphate from the aqueous humor or nutrient solution into the lens that there is an active transport of phosphate into the lens. Proof of this fact was obtained when Müller and Kleifeld (1953b) demonstrated the inhibitory power of KCN, iodine monoacetic acid, and NaF over the process. In spite of this, however, it is of course possible that a part of the inorganic P^{32} penetrates into the lens by diffusion. The inhibition brought about by the enzyme inhibitors does not depend on the diminution of the permeability of the capsule. Inasmuch as the enzyme inhibitors mentioned bring about an inhibition of the carbohydrate metabolism, it may be assumed that the assimilation of P^{32} is dependent on the energy supplied in the catabolism of carbohydrates. This is further substantiated by the observation that any inhibition of the assimilation occurs in

conjunction with a decrease in the absolute content of 7-minute hydrolyzable phosphate. When all the information relating to absorption is taken into consideration, it seems to show that there is a close connection between the adenosine triphosphate content of the lens and its capacity to absorb phosphates.

Since the epithelium of the lens must be regarded as the important site for the elaboration of adenosine triphosphate, it may be that there are different conditions for phosphate absorption at the front and at the back of the lens. Experiments designed to clarify this problem have shown that when the capsule and the epithelium are removed, the capability of the lens with regard to the active absorption of phosphate decreases. It must therefore be assumed that the location of the processes that bring about the active absorption of phosphates is to be found in the capsule-epithelium system. As these processes can be inhibited by KCN, NaF, and iodine monoacetic acid, they are probably closely connected with the oxidative catabolism of the carbohydrates. The dependence of the phosphate-absorption capability of the lens on its adenosine triphosphate content also favors this assumption. Studies on the isolated posterior capsule, however, seem to show that in the interplay between the posterior capsule and the lens fibers there are metabolic processes which can be disturbed by KCN and on which depend the absorption of P^{32} and its incorporation into adenosine triphosphate.

The changes in the carbohydrate metabolism that are bound up with age naturally go hand in hand with changes in the phosphate metabolism. Very detailed investigations into the behavior of the individual phosphoric acids in the lens have shown that all of them suffer a more or less marked decrease. Strikingly enough, although all the esters decrease by approximately the same percentage in the nucleus as in the cortex (only the inorganic phosphate behaves differently in this respect), this decrease is not distributed uniformly. Differences in the percentage decreases brought about by age in the individual phosphoric esters therefore, can not be entirely due to the fact that the carbohydrate metabolism of the lens becomes more restricted in scope as life goes on; there must also be some change in the actual course such metabolism follows. The nature of some of the differences found suggests that they are the result of changes in the carbohydrate catabolism. Knowledge of this fact serves to indicate the path to be taken in further studies of the changes produced by age in the phosphate metabolism of the lens.

Various types of cataract formation are known to be bound up with disturbances in the sugar metabolism. Similarly, disturbances in phosphate metabolism have also been seen in cataractous lenses. There are, however, certain definite differences in the course followed by the carbohydrate metabolism in cases of lens damage resulting from x-ray irradiation, galactose, alloxan diabetes, and naphthalene. Experiments carried out by the authors in animals show that the effect on the phosphate metabolism is also different in the case of naphthalene poisoning, alloxan diabetes, and dinitrophenol poisoning. Thus, it appears that an investigation of the phosphate metabolism offers great promise in regard to increasing our knowledge of the physiology and pathology of the crystalline lens.

Comment: The authors of this article have written a magnificent survey on phosphate metabolism both generally and specifically for the lens. As new enzyme systems are discovered and older physiologic processes are investigated more intensively, the group of compounds known as the organic phosphates is implicated more and more often. The most important member of this group is that ubiquitous substance, adenosine triphosphate or ATP. It has been found almost everywhere that a transfer of energy occurs in living tissue. This is true for plants and for all animals from ameba to man. This compound, as the name implies, has three phosphate groups, and it is in the linkage of these groups to each other that the great energy resides. Breaking one of two end linkages releases 12,000 calories of energy. Although many organic phosphates are unstable and release energy on hydrolysis, ATP possesses the further attribute that unless attacked by a specific enzyme, ATP is stable in water—an absolute essential for a substance usually found in soggy tissues. Small wonder that this substance has been investigated in such diverse systems as muscle contraction, nerve conduction, kidney function and lens metabolism. As the author points out, ATP is essential to normal lens metabolism, and there is some evidence that ATP levels in the lens do decrease early in cataract formation.

Unfortunately ATP is present only in minute amounts, but enzymic methods have been developed which measure as little as 0.02 μM of high energy phosphates. Such magnitudes are almost at the molecular level—where indeed such measurements must be made, if we recall that von Sallmann has shown that the initial change in radiation cataract may involve only 20 or 30 nuclei. As yet, it has not been possible to demonstrate a decrease in organic phosphates in the lens at a time when histologic changes are already apparent. (The interested reader will find a more detailed yet completely understandable discussion of ATP in the April 1953 issue of Scientific American. This magazine, incidentally, does an excellent job of making diverse scientific subjects comprehensible to the worker in a specialized field. For example, Dr. George Wald's fascinating article, "The Origin of Life," was published in the August 1954 issue.)

DAVID SHOCH

EFFECT OF HYALURONIDASE ON THE VISCOSITY OF THE AQUEOUS HUMOR

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Brit. J. Ophthal., 1956, *40:* 545–548

Bárnáy and Scotchbrook described a hyaluronidase-sensitive barrier to aqueous outflow in the angle of the anterior chamber of enucleated cattle eyes. Their conclusions were based on the observation that the addition of hyaluronidase to the perfusing fluid increased the rate of outflow.

Hyaluronic acid was demonstrated in bovine aqueous by Meyer and Palmer. Hyaluronidase has a specific action, reducing the viscosity of hyaluronic acid by a mechanism believed to consist in depolymerization followed by hydrolysis. The question therefore arises whether hyaluronic acid in the aqueous,

(rather than in the angle) of the eyes used by Bárány could have been the substrate. Although the anterior chambers were washed out before the readings were taken, residual hyaluronate could have produced the observed results. Finally, it is possible that a solution of hyaluronidase may have a detergent action, altering the rate of flow through the angle.

An experiment was accordingly planned to demonstrate the effect of both hyaluronidase and a wetting agent on the rate of flow of aqueous humor, under controlled conditions. These effects were noted in terms of change in viscosity. Viscosity is described as the "reciprocal of fluidity." Under controlled conditions, the rate of flow of a liquid is inversely proportional to its viscosity. An Ostwald viscosimeter pipette was used. A constant volume of liquid was allowed to flow by gravity through a small-bore glass tube. The length of time required for the liquid to flow is a relative measure of its viscosity. The relative viscosity of a liquid is the ratio of its flow-time to that of distilled water. Temperatures were kept within a range of 37 to 37.5°C.; preliminary observations had shown that variations of 0.5°C. did not affect the result.

Viscosity measurements were made of pooled aqueous, distilled water, normal saline, egg albumen solution, human serum, and vitreous solution. Hyaluronidase was added to each of these, and, in separate experiments, a detergent solution was added to most of them. It soon became evident that fresh aqueous behaved differently from aqueous taken from stored eyes. Consequently, cattle eyes were collected at the abattoir 1 hour post mortem and were divided into two lots. In the first lot, the viscosity determinations were made at once on half the aqueous withdrawn, and on the other half, which was stored at 40°C. they were made 7 days later. The eyes in the second lot were stored intact for seven days at 40°C. and then the aqueous was withdrawn and the viscosity measured.

Tabulation of the effects of the additives on fluids other than aqueous humor showed that the only significant change in viscosity followed the addition of hyaluronidase to the solution of vitreous humor (half vitreous and half distilled water). The detergent had no viscosity-reducing effect. A similar tabulation was made of the effects of the same two additives on the viscosity of bovine aqueous in various states of preservation, and on fresh rabbit and pooled human aqueous taken from otherwise normal human eyes at the time of cataract extraction. Again the results showed that the detergent had no effect. However, the viscosity of aqueous increased post mortem when stored in oculo, and this increase was significantly reduced by hyaluronidase. Storage in vitro did not alter the viscosity of aqueous.

These and other experiments indicate that changes in quantity of polymerized hyaluronate in the aqueous cannot explain Bárány's findings. It is, therefore, possible that polymerized hyaluronate is a part of the tissue of the angle, or that a "clot" of polymerized polysaccharide from the aqueous may be deposited in the drainage channels.

However, a post-mortem rise in the content of polymerized hyaluronate was found in the aqueous, indicating that there may still be a relation between

polymerized hyaluronate in the aqueous and certain pathological conditions, particularly glaucoma. It may be that the balance between polymerized and depolymerized hyaluronic acid in the tissues and fluids of the eye varies during life, and that this variation is a factor in the etiology of chronic simple glaucoma.

Comment: Bárány in the past several years has presented evidence that indicates that there is a polysaccharide barrier to aqueous outflow in the angle of the anterior chamber. On the basis of his imaginative studies it has been postulated that the site of obstruction in open angle glaucoma may be this hyaluronidase-sensitive barrier. However, there have been many objections to this theory. A major criticism has been that the substrate that Bárány is depolymerizing is in the aqueous rather than in the angle. Beswick and McCulloch effectively substantiate Bárány in this article. In passing they also show that up to 5½ hours post-mortem changes play little part in reducing viscosity and that the trauma of handling the excised eye also is ineffective. This paper adds solid evidence to Bárány's hypothesis that there is a polymerized hyaluronate in the chamber angle.

The recently published transactions of the first Josiah Macy conference on glaucoma presents Bárány's work in much detail with valuable commentary by the other members of the panel.

DAVID SHOCH

COLOR VISION

NEUTRAL POINTS IN 138 PROTANOPES AND DEUTERANOPES

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J. Optic. Soc. America, 1956, *46:* 640–649

A color-blind person who can secure hue matches for all lights with mixtures of only two lights of different spectral composition (serving as working primaries) is said to be dichromatic. Normal persons and anomalous trichromates must be allowed to use three primaries.

A dichromate can also match any "white" light with some mixture of his working primaries. On a chromaticity diagram, a straight line through the point representing this mixture and through the white point is an isocolor line. Any wavelength at which this line cuts the spectrum locus is an intraspectral "neutral point" of that dichromate—he can match light of that wavelength (or of that dominant wavelength) to the working white light simply by making a brightness match. A protanope, deuteranope, or tritanope has one intraspectral neutral point. A tetaranope is supposed to have two. The exact locations of average neutral points for these different kinds of dichromates are of the greatest theoretical importance. To be acceptable, a set of valence curves for the elementary chromatic sensations of any type of dichromasy, based upon whatever data, must so intersect as to display the neutral point. In the literature, neutral-point data determined on real subjects are scanty and variable. Rather than to try to use them, modern investigators seem to prefer theoretical values. Real neutral points, however, should be more useful, even for theoretical purposes, than any hypothetical ones, provided, of course, that they are reliable. Published data are generally unreliable because (1) they have been determined with reference to an unspecified white standard, or to one of such low color temperature as to be unrealistic, and (2) because they have been determined by methods which allow the subject's particular depth of lens coloration and macular pigmentation to influence them greatly, falsifying any theoretical analysis of color-visual phenomena in terms of fundamental receptoral properties.

In their search for a physiological white standard, the authors used CIE Illuminant C (6500°K) for much of their work, finally abandoning it in favor of NBS Illuminant D (7500°K). The subjects mixed blue and green Munsell paper disks to match a neutral pair, the dominant wavelength of the blue-green then being the neutral point which is little affected by ocular pigmentation, since the latter shifts the chromaticities of both the chromatic and the

neutral papers. Illuminant C neutral points were determined for 58 protanopes and 52 deuteranopes, but reason was found for excluding 19 of the protanopes and 14 of the deuteranopes (measured earlier by Walls and Mathews) from the averages. The neutral point range of the 39 new protanopes is λ490.9–494.6 mμ, with the mean at 492.3 (S.D. 0.70). The range for the 38 new deuteranopes is λ495.9–501.7 mμ, mean 498.4 (S.D. 1.21). These means are closer together than the hypothetical neutral points (of the CIE standard observer). Nevertheless, the gap between all protanopes and all deuteranopes is real.

Illuminant D neutral points of 13 other protanopes range from λ488.7 to 492.0 mμ, mean 490.3 (S.D. 1.05); those of 15 other deuteranopes from λ493.7 to 498.8 mμ, mean 496.2 (S.D. 1.25). The "D" ranges are thus smaller than the "C," the means are at shorter wavelengths and are still closer together, but the intergroup gap remains and is not smaller. Therefore, it is possible, after all, to tell a protanope from a deuteranope by the location of his neutral point.

From the findings obtained in this study, it may be concluded that NBS Illuminant D is certainly not "too blue" and is even a more perfectly neutral white standard for physiological work than CIE Illuminant C.

Comment: This is a piece of work of the very first class and seeing the name of the senior author on its title page no would expect, or be satisfied with, less. While this reviewer could never fully subscribe to the views on color vision theory promulgated or defended by Gordon Walls, he will never fail to turn a respectful and receptive ear to any of his pronouncements. There is hardly any one in this field today whose knowledge would be as deep and extensive and whose criticism as penetrating as that of the senior author of this extremely important paper. We can certainly throw all previous studies about this subject overboard, and since Walls and Heath in this paper have so demonstrated, accept as definitive that protanopes and deuteranopes have different neutral points with no overlap of regions. This is extremely important to know, as it offers a criterion, as simple as it is unequivocal, for the differentiation of the two conditions.

Of very great value for the whole field of color physiology are the authors' experiences with Illum in ants C and D and their remarks about the appearance of these two illuminants to normals and dichromats. Certainly, no color studies with lights or low color temperature will be acceptable in future quantitative work.

Another important contribution is the authors' study on the technique of neutral point determination. They show that determinations with Munsell papers (color disks, in general) are preferable to those with monochromatic and mixed spectrum lights. The latter technique will not eliminate the influence of biologic pigmentation in lens and macula, and the power will not be affected by it. Students of the history of this subject should be interested in seeing how closely our authors' findings agree with the beautiful and accurate data of Pitt.

ARTHUR LINKSZ

OPTICS

WHAT DO WE SEE STRAIGHT?

M. C. COLENBRANDER

Leyden, The Netherlands

Ophthalmologica, 1956, *132:* 291–294

The architrave of the Parthenon is not straight, but arched slightly upwards. And yet we see it as straight. Architects tell us that this is because the Greeks knew something we have forgotten, that is, that a horizontal line above the horizon must curve upwards in order to appear straight, and that a straight line looks sagged. This is a problem of sensorial physiology and, consequently, also one of interest to ophthalmologists.

Everyone agrees that the architrave of the Parthenon appears to be straight. But this does not justify the general conclusion that straight lines look sagged. Roof-gutters in rows of houses make a perfectly straight impression, and no one thinks of them as sagged. The explanation of this remarkable phenomenon seems to lie in two tendencies, first, the tendency to see nearly straight lines as straight, and, second, the tendency to see acute angles wider and obtuse angles narrower than they are, and consequently to accord to them a greater similarity to right angles. The first tendency is based on the wish to supplement incomplete data and to make an adequate entity of them. This also occurs in other respects. We guess the correct meaning of words almost without realizing it. Sentences that are imperfectly understood or only partly pronounced are completed from the context. In certain works of art, details that might be misleading are often omitted, while other works, such as Rembrandt's etchings, for example, contain tangles of lines from which the mind intuitively selects those that make up the picture. In the same way, we are willing to see a curved line as straight when we are convinced that a straight line is what we are meant to see. Thus, we see the curved line of the architrave as straight because we want it to appear straight.

This, however, does not explain why the Greeks built the architrave curved. The solution seems to lie in the desire to see angles more like right angles than they really are. This doubtless is related to the fact that, on account of perspective distortion, the right angles of our surroundings are not as a rule reproduced on the retina in the form of right angles. We so easily try to convince ourselves that even the most obtuse and the most acute angles are right angles in perspective distortion. Nearly every flat reproduction gives examples of this phenomenon, which was used effectively by Ames in his Distorted Room. The room is not straight, but if it is viewed from a certain place it produces the same perspective picture as a straight room. The tendency to see angles as squarer than they are is the basis of many optical illusions. For instance, the oblique line

passing behind a beam; the parallel lines, which, because of oblique hatchings against each other, look as if they are not parallel. The lines influence each other mutually—when the hatchings are made at an angle of 90° to the parallel lines, the hatching lines *apparently* are not at right angles.

In the Parthenon, the slanting sides of the tympanon influence the architrave just as the hatchings influence the parallel lines. The architrave would, therefore, appear sagged if it were straight, just as it appears straight now that it is convex.

The Parthenon shows three other peculiarities, each based on a different principle. The first, which makes the building look larger than it really is, is the imperceptible upward tapering of the columns. By this, the thinner, upper part is projected to a greater than actual distance, so that the columns look taller than they really are. The second is based on the principle that irradiation makes dark objects look smaller against a dark background than against a light one. This was taken into account by the architect of the Parthenon. The corner columns, which are usually seen against the background of the sky, are slightly broader than the others. The third peculiarity satisfies the requirement that a building should give an impression of firmness. A sagging architrave looks too weak to bear what rests on it, but an arched one suggests tension, and ability to bear weight. On these grounds, also, a convex architrave is preferable to a sagging one. The floor on which the Parthenon stands also bulges slightly, probably for the same reason.

A column must bear not only its burden but also its own weight. That is why a conical upward-tapering column is to be preferred to one that tapers downward. A roof slanting on both sides suggests that the main support is under the central line and that the two sides tend to lean inwards. To prevent this, the outer columns diverge slightly upwards, like the pegs of a tent.

In comparison with the harmony and strength exhibited by the damaged Parthenon, the Madeleine and the Chambre des Députés in Paris, in which everything is straight, appear lifeless.

The unprejudiced knowledge of the human mind, which is so clearly shown in this majestic building, is awe-inspiring.

Comment: This reviewer is certainly pleased to find another ophthalmologist interested in such "impractical" problems as the appearance of the architrave of the Parthenon, the great Athenian temple whose consummate beauty has never been yet surpassed in some twenty-four centuries. Colenbrander gives a near explanation for the apparent straightness of the actually curved architrave and his explanation is not only pleasing but quite plausible. Our misjudgment of its curvature would thus be just another example of optical illusions well known to students of psychology and shown recently in their full impressiveness in the so-called distorted rooms of Ames. Probably not many will have the chance to see the Parthenon itself, but this reviewer has been told that a replica of it exists in this country, in Tennessee, and it would be good if perchance a reader of this review would once more turn an appreciative eye upon this replica. Possibly another reader might also perchance turn an eye upon the architrave of the famous, beautiful Madeleine which not many have so far found "lifeless" as our author did.

Quite interesting are Colenbrander's other apercus—on the arched appearance of the horizon, on the tapering of the columns of the Parthenon and the "technician's conscience" and the irradiation by which "dark objects look smaller against a dark background than against a light one." And one will gladly repeat his last sentence: "Indeed, the unprejudiced knowledge of the human mind, which is so clearly shown in this majestic building, is awe-inspiring."

ARTHUR LINKSZ

PSYCHOLOGY

RELEARNING TESTS FOR INTEROCULAR TRANSFER FOLLOWING DIVISION OF OPTIC CHIASMA AND CORPUS CALLOSUM IN CATS

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J. Comp. & Physiol. Psychol., 1956, *49:* 529–533

It has been found that pattern discriminations learned with one eye transfer readily to the untrained eye in cats that have had the optic chiasma divided in the midsaggital plane. If, in addition, the hemispheres have been separated by section of the corpus callosum, the discrimination performance drops to a chance level as soon as the blinder is shifted to the trained eye. The performance then remains at or near chance throughout 40 to 80 test trials with the untrained eye, suggesting complete amnesia for the habit learned with the first eye. Further, in these cats with chiasma and callosum both sectioned, opposing discrimination responses, normally incompatible, can be learned independently with right and left eyes respectively. Together, the findings suggest that the interocular transfer in chiasma-sectioned cats is mediated centrally by the corpus callosumnd can not be obtained with the callosum sectioned.

The present investigation was undertaken to test the possibility that some latent transfer that remained undetected under the above conditions might be revealed in more rapid relearning of the discrimination with the second eye. The general plan was to compare the monocular learning of a series of visual discriminations with the relearning of the same discriminations through the other eye in cats with chiasma and callosum both sectioned.

Six cats were used, ranging in age from five to ten months at the start of the experiment. They were brought into the laboratory from various sources at ages ranging from two to eight months. The chiasma was sectioned first and then the callosum with an interval varying from 5 to 26 days between first and second

operations. A minimum of four weeks was allowed for recovery from the second operation before training was started.

A darkened discrimination box was used in which the cats were trained to choose the correct one of two translucent patterns placed side by side in swinging doors at the end of the box. Correct responses were rewarded with a morsel of food; incorrect responses activated a buzzer. One eye was kept covered by a rubber mask. An attempt was made to select pairs of patterns that were quite dissimilar in order to avoid carry-over of generalization or interference effects from earlier to later learning tasks.

The training schedule involved five daily sessions per week of 50 to 60 trials as a rule, though as many as 90 trials were given occasionally. The patterns were alternated from left to right except when it became necessary to break a position habit.

The results of the main series of tests are generally opposed to any visual transfer. The positive saving scores are small in all cases, not exceeding 21 per cent, and they are counterweighted by negative saving scores of approximately the same or greater magnitude. The difference in learning scores for first and second eyes is well within the range of normal variation that one commonly sees in the learning of the same problem by different cats or in the learning of differetn problems of similar difficulty by the same cat.

Taken as a whole, the findings point to the conclusion that visual mnemonic effects implanted through one eye under the above experimental conditions are inaccessible when the other eye is used. In other words, the function of the two hemispheres with respect to visual learning and memory remains entirely independent. The present results do not exclude the possibility of interocular transfer under other conditions as, for example, after excessive overtraining to a high level of automaticity. Particularly in the case of brightness discrimination, (which is still present after removal of striate cortex in the cat), one might expect to find conditions that would make transfer possible at the subcortical level. Finally, it is interesting that the learning curves for left and right hemispheres of the same animal, despite their independence and individual variation, are found to be much more alike in character than are those from different animals.

Comment: This significant research contributes definitively to the understanding of neuroanatomical bases for psychological aspects of form recognition. The results are in agreement with other evidence to the effect that form vision, where a learned response to visual patterns is involved, is strictly a cortical function in mammals. Apparently midbrain visual centers and their commissural connections contributed nothing toward a mediation of ocular equivalence so far as the recognition of these visual stimulus patterns is concerned. The authors indicate that these preparations will be given other kinds of tests. We might expect that a discrimination habit based on total luminous flux should show transfer. A technique such as that used by Heinrich Klüver to eliminate need for spatial vision would be appropriate. Some procedures requiring brightness discrimination do not eliminate the spatial aspect, and therefore, might also result in failure of interocular transfer.

The use of binocular cues for depth might be measured by employing prisms. Although

such tests apparently have not been used before with cats, their effective adaptation by Eckhard Hess for research on the vision of birds suggests their feasibility. Hess demonstrated that binocular vision is of considerable importance in the depth perception of his animals. The present research opens a new avenue of approach to the study of binocular as well as interocular functions.

An earlier issue of the *Survey of Ophthalmology* (1956, *1:* 91–93) carried an article that described another technique for disrupting the functional equivalence of the eyes in visual recognition. In that study Chow and Nissen deprived infant chimpanzees of form vision and found that the first visual habits learned monocularly also failed to transfer. However, unlike the findings of Sperry, Stamm and Miner, there was a "saving" in trials to learn by the second eye. This would suggest that the isolation of visual function was less complete or only temporary. One is tempted to speculate as to the possible relations between these two kinds of procedures and the condition of amblyopia ex anopsia in man. A central isolation of input from each eye is apparently involved, but the mechanism of solationis hardly to be considered the same in every respect. The procedure of Chow and Nissen holds more analogies with the clinical problem.

AUSTIN RIESEN

REMARKS ON LIPEMIA RETINALIS OCCURRING IN A CASE OF DIABETES MELLITUS

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Philadelphia Medical Times, 1880, *10:* 318–319

It is well known that diabetes mellitus is frequently accompanied by abnormal conditions of the eye: this fact was noticed far back in pre-ophthalmoscopic times. Rollo, in his monograph on Diabetes, London, 1798, refers to two cases of the kind, probably the first mentioned in literature in which there is reason to infer that the diabetes was the cause of the eye affection. It is true that Blankaart, of Amsterdam, in 1688, mentions the occurrence of blindness in a case of diabetes; whether the case were one of diabetes mellitus or insipidus does not appear. Possibly Blankaart was unaware of the distinction, as it was only fourteen years previously that Thomas Willis called attention to the sweet taste of the urine of certain cases of diabetes. However, as Blankaart ascribes the blindness of his case to a tumor found after death pressing upon the optic nerves, we must look upon the blindness rather as a coincidence than a sequel of the diabetes. Since Rollo's time numerous instances of eye affection in diabetes mellitus have been observed, and in later years the ophthalmoscope has enabled us to study them more closely. These eye affections are disturbances of refraction and accommodation, lens opacities, vitreous clouds and hemorrhages, certain affections of the optic nerve, and certain affections of sight apparently depending on central lesions. It is, however, to none of these that I invite attention tonight. The appearance I bring before you has, I believe, never been described or copied.

The patient from whom this picture was copied was an inmate of the male medical ward of the Episcopal Hospital, under the care of Dr. Louis Starr. Owing to his complaining of defective vision, I was asked to examine his eyes. I saw him for the first time November 11, 1879. Examination, under atropia, revealed a nuclear cataract, with partial involvement of the cortical, on each side. The appearance of the fundus of each eye was quite peculiar; that of the left was more visible than that of the right, owing to the left lens being less involved than the right; still the right fundus was clearly enough visible. The peculiar appearance which attracted my attention was the color of the blood-vessels. Those of you who are familiar with the normal fundus know that one of the most striking objects seen in ophthalmoscopic examination is the retinal vessels,—that the retinal veins are characterized by their larger size and the dark color of their blood, the arteries being smaller and lighter in color. In the

picture of the fundus which I present to you, you will notice at once a great difference from the normal appearance. The vessels are very light in color, both veins and arteries, and the color very closely approximates that of the fundus; the veins are very large in size, and at the same time not tortuous; the artery is seen branching off from the trunk and running downward and inward for a short distance, and is then lost, by reason partly of similarity of color, in the fundus. Whether a branch also ran upward could not be told. A vessel in the upper half of the fundus is seen stopping, apparently, at the edge of the excavation; it could not be traced farther: very possibly it was a branch of the artery.

The color of the vessels is represented as they appeared when the light was thrown on them directly; when the mirror was shifted by a slight rotary motion the veins could be distinguished by their slightly darker color. There was no retinitis in either eye, nor were any hemorrhages seen.

I will now pass around this accurate painting of the fundus of the right eye; it was very skilfully copied for me by my friend Dr. Nancrede, and recalls the case very vividly to my mind. While the picture is being examined we may briefly discuss its nature.

1. Was it due to any structual change in the vessel-coats, by reason of which the contained blood was partially obscured from sight? There are morbid processes which attack the tunica adventitia of the vessels, which may almost render the blood invisible to the eye. The appearance of this condition is totally different from that under consideration. Those acquainted with the two could not mistake the one for the other.

2. We may, then, turn to the character of the blood itself. To be as brief as possible,—for I am only presenting this picture, not attempting to do more,—the blood was examined: the finger was pricked, and a small quantity of blood obtained. The character of the blood was very peculiar: it had a milky-red hue, approximating that of a piece of pink coral. Examination with the microscope revealed the presence of fat globules. The number of red globules was carefully counted by Dr. F. P. Henry, and it was found that the blood was not leucocythemic. This was, therefore, one of those cases of diabetes mellitus accompanied by lipemia, or a condition of blood characterized by a milky hue, arising from the presence of an abnormal quantity of fat. Cases of the kind have been described by Virchow, Griesinger, Kussmaul, Sanders, and others.

This peculiar appearance of the retinal vessels was then, doubtless, due to abnormal presence of fat in the blood, and I may properly apply to it the name of retinal lipemia.

I have thus presented to your notice this picture of the fundus oculi of this case, without going into the details. The condition is interesting from its novelty, but it may also have some practical bearings. Without, however, alluding, at this time, to points which might be of interest to the specialist, I have presented this picture as showing one feature of an obscure complication of an obscure disease. I thought also it would be of some interest to the Society, as the attention of the profession has recently been called to this condition of lipemia in diabetes mellitus: I refer to the able and interesting paper on Lipemia in Diabetes Mellitus

and Fat Embolism, written by Professor Sanders and Mr. Hamilton, published in the Edinburg Medical Journal for last July.

Editorial comment.—Since Heyl first described lipemia retinalis some 80 cases have been reported, including 14 in nondiabetics. Lipemia retinalis comes from a very excessive concentration of neutral fats in the blood, the other lipids being of no significance in this connection. In normal serum the neutral fat content ranges from zero to 150 mg. per 100 cc. according to the stage of digestion. The serum assumes a milky appearance when the concentration of neutral fat reaches 0.5 per cent, but lipemia retinalis is only seen with a neutral fat content of over 2.5 per cent and disappears when the level falls below 2 per cent. In lipemia retinalis the milky appearance of the arteries and veins is first seen in the far periphery and gradually extends centrally to the disk. The arteries and veins then become difficult to differentiate and the vessels appear larger and ribbon-shaped. As less sugar is utilized in diabetes more fat is mobilized from the storage depots for migration to the liver. Insulin reverses the process by making sugar available for combustion; fat then disappears from the blood and liver and returns to the storage depots. In a diabetic, lipemia retinalis indicates poor control of the disease, but the condition in itself causes no organic damage to the retina nor any disturbance of retinal function. This transportation hyperlipemia may occur also in chronic alcoholism, severe anemias and leukemia, lipid nephrosis, and poisoning by phosphorus, chloroform and carbon tetrachloride. Lipemia retinalis may also occur in retention hyperlipemia where the mechanism by which the blood fat is removed to the storage depots is disturbed. In these cases the lipemia retinalis disappears by drastically reducing the fat in the diet; insulin, in this situation, does not affect the level of blood fat.

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Biographical Note

Albert Gallatin Heyl (1847–1895) was born in Philadelphia and attended the University of Pennsylvania, from which he received his medical degree in 1870. After a year of internship he devoted the next three years to the postgraduate study of ophthalmology in London, Heidelberg, and Vienna. On his return to Philadelphia he was appointed to the eye staff of the Episcopal Hospital, becoming in time Senior Ophthalmic Surgeon. In 1886 he also joined the Pennsylvania Eye and Ear Infirmary, a private, free dispensary supported by Dr. George Strawbridge. He was regarded as a brilliant eye surgeon. A profound student, he contributed numerous papers to the Transactions of the American Ophthalmological Society and other publications, the most important being on uremic amblyopia, hyphema, coloboma lentis, metastatic tenonitis, intraocular lipemia, acute glaucoma induced by duboisin, operative treatment of glaucoma, diffusion circles of ametropia, and spontaneous rupture of the choroid. According to S. D. Risley, who was his colleague for 10 years, he was very much of a recluse.

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Reports from Abroad

SOUTH AFRICA

Ophthalmology is the oldest specialty in Southern Africa. D. J. Wood, the distinguished ophthalmologist, commenced practice in Cape Town in 1893. He was the first to confine his practice to a specialty. Sixty-three years later there are just over 100 ophthalmologists on the statutory register of specialists. Mostly in the large towns, they serve a population of 14 million (last census—whites 2,907,000, Africans 9,306,000, Asiatics 421,000 and colored 1,281,000.

The vast variations in the environmental conditions to which the different races are exposed produce marked racial difference in disease incidence. Most of the nonwhites live under very poor socio-economic conditions; extreme poverty, poor housing, malnutrition, and bad health conditions generally obtain. There is an appallingly high incidence of tuberculosis among them. Phylctenular disease producing severe corneal scarring, is rampant in the young, adding to the later difficulty of differentiating the corneal opacities that are so common in South Africa.

Blumenthal has helped to elucidate this problem of corneal disease. He has described a disabling corneal disease which is distressingly common in the native areas of the Eastern Cape Province and Transkei. Bantu mothers breast feed their babies to a relatively late age, 2 years being a fair average. The weaned child is then fed on a purely carbohydrate diet—mealiemeal, completely deficient in protein, fat, calcium, iron, vitamin B complex and ascorbic acid. Not until the child goes foraging for himself (at about the age of 5) with older children for roots and berries, birds and their eggs, small animals and insects, does he find the necessary vitamins and trace elements. During this 2- to 5-year period, there occurs (a) generalized corneal stromal softening, followed later by bulging of the cornea in whole or in part, and the formation of various types of staphyloma or ectasia a few years later, without any signs of infection; or (b) rapid, localized, corneal liquefaction or lysis, usually with a painless perforation and clean prolapse of the iris, also with an absence of infection. A notable feature often seen a few years later is the remarkable symmetry of the lesions; an adherent leukoma at or near the limbus at 5 o'clock, right eye is mirror-imaged by one at 7 o'clock, left eye. In other cases the pupil is a thin horizontal slit, being adherent to the cornea at 3 and 9 o'clock. Blumenthal has named this entity malnutritional keratoconjunctivitis, but a better name many be malnutritional keratopathy.

Only a decade ago, trachoma was thought to be rare in South Africa. However it is extremely prevalent in the Northern Transvaal, and in certain parts of the North Western Cape. In some Transvaal native reserves where the Africans are living under primeval conditions, 90 per cent show signs of it. In older patients it is the commonest cause of blindness, due to entropion trichiasis and corneal scarring, but trichiasis can be found in children of 4 and 5 years of age, which is unusual. The Bureau for Prevention of Blindness of the South African National

Council for the Blind runs a mobile field clinic for the treatment of these cases, spending from 3 to 4 weeks in the area. In the field scores (sometimes over 100) of entropion operations and, in cases of bilateral cataracts, many lens extractions are performed. Graham Scott and Taylor are running a 3-year experiment to try to control trachoma by the compulsory instillation, during the summer fly months, of antibiotic ointment daily in all children from 0 to 5 years of age. The idea is to reduce the pool of infection in the youngsters, to eliminate secondary infection, especially by Koch-Weeks bacillus, and thus leave the flies no organisms to spread to the new-born babies. Four villages in the Northern Transvaal are participating in this experiment; local inhabitants do the instillations.

Syphilitic eye lesions are common in the Bantu and Colored. Optic atrophy and choroido-retinitis are not infrequent; interstitial keratitis is very common.

Hydatid cyst and gumma of the orbit must be considered in all orbital swellings in Southern Africa.

Glaucoma in the Bantu is a real problem. It is usually painless, chronic and by the time they present for treatment one eye is blind, and the other has a tubular field, and cupped atrophic discs. There is no noticeable response to miotics or filtering operations. Acute primary glaucoma is rare though acute secondary glaucoma is frequent, on account of the frequency of ocular trauma. Despite this high incidence of trauma to the eye, sympathetic ophthalmia does not raise any problem. Contrary to current teaching, multiple sclerosis can and does occur in South Africa, but unlike in Europe, is very rare. Confirmed cases of toxoplasmosis causing central choroido-retinitis have occurred.

Retrolental fibroplasia is exceedingly rare; a few cases have been reported in Johannesburg, but only one case has ever been seen in Cape Town.

Central Serous Retinopathy can be caused by Rift Valley fever. This little known disease has occurred in South Africa during the autumn of 1951 and 1953, and again this April (1956) in the Orange Free State killing numerous sheep and infecting more than 200 human beings in one area.

Rift Valley Fever (enzootic hepatitis) is a specific virus infection producing fatal epizootics in sheep and cattle, associated with a characteristic eosinophilic degeneration of the parenchymal cells of the liver. In man it causes a dengue-like fever which is almost never fatal. It is one of a large group of tropical diseases transmitted by mosquitoes. *Aedes* (*Ochlerotatus*) *Caballus Theobald*, a pan breeder, has been identified as the vector in South Africa, but this mode of infection of man is relatively rare. Man usually acquires the infection by contact with the meat or tissues of animals dead from Rift Valley fever. Thus it is liable to infect veterinary surgeons, farmers and their laborers, who in the course of their work carry out postmortem examinations on dead sheep and cattle. Butchers, housewives and their servants also acquire the infection by handling infected meat.

The disease is generally free of complications and often is considered to be influenza. The most important complications are ocular. Macular edema, accompanied occasionally by small hemorrhages (Schrire and Freed) occurs a few days to a few weeks after the pyrexial attack. This produces a central scotoma

with consequent depression of the central visual acuity. With the subsidence of the edema the vision has generally returned to normal, but in some cases has remained permanently impaired. Retinal detachment has been encountered.

This disease was first described in 1931 on a farm in the Rift Valley on the shores of Lake Naivasha in Kenya—amongst lambs and cattle. Since then it has been described in Uganda, Southern Anglo-Sudan, French Sudan and French Equatorial Africa but is not confined to the Rift Valley, since it has been reported in Japan.

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Cape Town, South Africa

Book Reviews

"Physiology of the Ocular and Cerebrospinal Fluids," by Hugh Davson (*Little, Brown & Co., 388 pp., 109 figures, $14.00*), *presents a physiologist's view of a subject which has been largely investigated by clinicians. It is reviewed here by H. Saul Sugar who is a contributing editor to the Survey of Ophthalmology.*

Davson, a physiologist, has presented a scholarly, encyclopedic treatise on the ocular and cerebrospinal fluids at a time when the physiology of the aqueous humor is being studied with great interest, both clinically and in the laboratory. At the same time many of the fundamental processes have not been completely worked out so that controversy is marked, as shown by the differences of opinion between the author and the "American" school led by Kinsey and Grant. The comparisons between aqueous humor and cerebrospinal fluid can not help but be stimulating to those specialists involved with the respective organs.

Davson introduces his work with two chapters on the anatomy of the pathways of aqueous and cerebrospinal circulation. These chapters are quite complete. Mentioned, especially in relation to the comparisons between the two fluid systems, are the Pacchionian-like bodies projecting into the lumen of the human Schlemm's canal. The embryologic aspects of the cerebrospinal fluid pathways is dealt with in considerable degree.

The major portion of the book (Chapters III through VIII) concerns the chemical composition of the two fluids in relation to their mode of production. Introductory material concerning measurement of distribution ratios, the Gibbs-Donnan equilibrium and the definition of secretion help the clinical ophthalmologist to understand the more technical aspects. Despite controversial interpretations, a mass of material of immense reference value is presented.

The final chapter concerns itself with fluid-pressures. Here again the material is introduced by general consideration of the subject in relation to both the eye and cerebrospinal system.

The vascular pulses, monometry, tonometry, and the factors influencing the normal intraocular pressure are discussed. The action of the drugs which influence the intraocular pressure are considered.

This book will certainly be of great interest to ophthalmologists concerned with the aqueous humor, especially from a research point of view, and to neurologists and neurosurgeons from the physiologic aspects. However, the reviewer can not help but point out the author's failure to consider the posterior chamber aqueous humor, a point which may be serious.

"Glaucoma, Transactions of the first conference," edited by Frank W. Newell (*Josiah Macy, Jr. Foundation. 251 pp., 65 figures, $4.50*), *is a nearly verbatim report of a general discussion concerning several aspects of glaucoma.*

It is reviewed here by Dr. P. Robb McDonald of the Survey of Ophthalmology editorial staff.

This small book reports the informal discussions on the subject of glaucoma by a representative group of ophthalmologists. Conferences of a similar nature concerning other fields of medicine have been previously sponsored by the Josiah Macy, Jr. Foundation.

The first part of the discussion is concerned with angle closure glaucoma. It is interesting to read the arguments pro and con the use of the terminology "angle closure glaucoma" and "narrow angle glaucoma," as well as about the possible mechanisms that may lead to the increased intraocular pressure. It was generally concluded that the increased tension of angle closure glaucoma is on the basis of the iris root blocking the flow of aqueous through the trabecula and that a relative pupillary block is the primary basis of the mechanism involved. Of secondary importance was pupillary dilatation.

The various trigger mechanisms leading to an attack are discussed, as well as the possible physiologic basis for the increase in intraocular pressure. Psychological influences may lead to vascular changes in the choroid and ciliary body, which in turn may initiate an acute attack of glaucoma.

The second chapter deals with the central control of intraocular pressure. Von Sallmann reported on experiments in which the intraocular pressure and blood pressure were recorded simultaneously. The response to drugs and stimulation of the hypothalamus were discussed by the various participants.

The discussion of the third chapter was headed by Bárány and dealt with the physiologic and pharmacologic factors influencing the resistance to aqueous outflow. The experiments dealt with the chemical dissection of the trabecular meshwork and the regulation of the resistance of the trabecular meshwork. This is a most intriguing and exciting approach to the problem of chronic glaucoma.

Unfortunately this volume can not be adequately reviewed. It records verbatim the remarks and questions of the various participants and no attempt is made to summarize the conclusions. It should be read by all those interested in understanding the physiologic basis of glaucoma as well as by physiologists interested in the formation and control of body fluids.

"Children's Eye Problems," by Emanuel Krimsky (*Grune and Stratton, 175 pp., 36 figures, $6.00*), *is reviewed here by Dr. F. H. Wright who is Professor and Chairman of the Department of Pediatrics at the University of Chicago.*

The author of this short handbook sets himself the difficult task of providing a guide for the various types of professional people who are concerned with children's eyes. He seeks to epitomize symptomatology, physiology, and management for the school nurse, the psychologist, the general practitioner, the psychiatrist, and the pediatrician, while at the same time offering the ophthalmologist an understanding of the medical and psychologic implications of eye disorders. The objective is too ambitious for a small book and the result will be satisfying only to the superficial reader. A more inquisitive one will use it mainly for the

references which are appended to the author's conclusions derived from personal experience and survey of the literature. The writing is spotty and is liberally interspersed with direct quotations from key references. The physical characteristics of the book are generally good with clear, appropriate illustrations and a satisfying index. The clean reproduction of the text is marred by occasional lapses in proof-reading.

"Neurology of the Ocular Muscles," by David G. Cogan (*Charles C Thomas. 296 pp., 86 figures, $8.50*), *is the second edition of an ophthalmic classic which has long been out of print. It is reviewed here by John Woodworth Henderson of the University of Michigan ophthalmology staff.*

This monograph on the neurology concerning the ocular muscles remains at the same high plane of excellence as the first edition. In addition, revision and addition of material on the ocular myopathies, together with more complete data on cerebellar function, has increased the name of the second edition. The inclusion of additional illustrations, especially the beautiful color plate by Dr. David Donaldson, makes the reviewer wish that the present high cost of color plates did not deter their more extensive use. The bibliography alone is worth the purchase price.

Cogan's presentation of the anatomy and action of the ocular muscles, omitting a division into "primary" and "secondary" functions, with a clear, non-diagrammatic presentation of "yoke" action, should be of value to all who instruct under-graduate students. The usual Junior student who has categorically memorized actions from the primary position often has difficulty in shifting to the more useful concepts of "yoke" action. The author states that "the terminology for movements of the eyes . . . is confusing," but fails to utilize the Lancaster terminology of directions, versions and vergences which has gained such widespread use among myologists and orthoptists. He still uses the terms of adduction and abduction instead of prism vergences, whereas these terms should be reserved for monocular movement. The inclusion of Breinin and Molduver's tracing of reciprocal innervation by electromyography is a distinct addition. The section on clinical testing of ocular muscles is concise and well-organized, including the discussion of diplopia testing and head position, but no mention is made of the Lancaster red-green test which is of much value in making serial records of paresis, together with diagnosis of mixed palsies and secondary contractures.

The sources of tonus to the extraocular muscles are discussed as the labyrinth, the kinesthetic sense, the retinas, and the higher cerebral centers. The question of whether or not there is true proprioception in the extraocular muscles is thoroughly discussed, and remains unresolved. However, as always, much of the reasoning against active proprioceptive function is based on lack of consciousness of such function—whereas much of the lower system of stretch reflexes in the cord does not anatomically reach a cortical arc to consciousness.

The presentation of the pharmacology, physiology and histology and its immediate application to the myopathies is of decided value. The recent use of

Tensilon in the diagnosis of myasthenia is omitted, together with the fact that in a true myasthenia gravis the atropine may be omitted in a diagnostic test with prostigmine if the diagnosis seems certain. Ophthalmoplegia externa is presented as an abiotrophy rather than a nuclear disease and the problem of surgical treatment of ptosis when both levator and orbicularis are involved is in accord with the reviewer's experience. (The safest procedure seems to be a tantalum sling which can be removed if corneal exposure becomes intolerable. Ed.) The confused state of knowledge with regard to the entity of dysthyroid exophthalmos is pointed out. (Contrary to the author, an excess of thylotropic hormone *has* been found in come cases of this disease, but not in all of them. The differentiation between the two types has been abandoned by some writers and the entire disease considered as one of degree. Not all of the cases regress eventually, but may reach a peak and remain there. The prognosis for vision when there has been optic nerve involvement by acute congestion is not always good, and the possibility of secondary glaucoma complicating the picture is not mentioned.)

Cogan is inclined to accept nuclear localization of oculomotor nerve function as shown by recent Horsley-Clarke experiments, discarding older work utilizing retrograde chromatolysis as less accurate. However, it is difficult to understand the loss of upward gaze in pinealoma cases where the rostral tectum is involved, whereas directly beneath this area the nuclei for downward gaze are located by the Horsley-Clarke technique—and anatomically this reasoning could be carried farther.

The list of clinical entities producing ophthalmoplegia is extremely well organized and offers a comprehensive list of etiologies. However, arterial aneurysms do not always have to rupture to produce oculomotor palsies, and some are certainly due to expanding pressure rather than by subarachnoid bleeding. The headache can also be localized as well as generalized, although recent rupture is more likely to produce a non-localizing headache. The author has wisely omitted any mention of lateralizing value of 3rd nerve palsy in tentorial herniation of the temporal lobe in supratentorial expanding lesions since this may frequently be misleading. The phenomenon of aberrant third nerve regeneration is particularly well discussed. In attributing to the larger intracranial course the lack of localizing value of abducens palsy, one notes that this should be qualified as the longer "exposed" intracranial course. (This stems from an experience with such a question given on the Home Study Course, where the reviewer found to his consternation that the students quoted a considerably longer measurement for the trochlea from Wolff's anatomy.)

The chapters on supranuclear connections concerned with eye movement are extremely well done and there is certainly no comparable summary of knowledge in the literature. Dr. Cogan draws on his extensive clinical experience especially in median longitudinal fasciculus lesions and the dissociated movements with cortical and subcortical lesions. However, even though the point is stressed from time to time, the reader must recall that much of the material is based on experiments in a variety of vertebrates, and cannot always be carried to man. (In support of localization of supranuclear upward gaze to the superior colliculi and

of downward gaze to the inferior colliculi is the further observation that where a pinealoma has progressed to involve first upward gaze and then downward gaze there may be an associated decrease in hearing. The retention of convergence when only upward gaze is involved may be noted in almost every pinealoma case by a peculiar nystagmoid type of convergent jerking of the eyes on voluntary upward gaze. One should add to the list of causes of weakness of upward gaze the natural decrease in such function in the elderly patient.)

The author's discussion of the location of a pontine center for lateral gaze notes that the 6th nerve nucleus lacks sufficient cells to account for a major contribution to the median longitudinal fasciculus system. This also holds true for the para-abducens nucleus. The vestibular nucleus concerned with eye movements does indeed furnish the necessary cellular component, but certain cases in which vestibular responses in eye movement are intact whereas the supranuclear pathway appears involved clinically at the same anatomical level cast doubt even on this thesis. One wonders whether "centers" are necessary or whether the involvement of supranuclear fibers in course is adequate to explain clinical findings.

To the discussion on convergence and divergence function might be added the recent work of Breinin demonstrating an active burst of impulses via the lateral recti during the divergence of intermittent exotropia. This appears to be the best evidence yet available in man of an active divergence mechanism.

The new material on cerebellar relations to ocular movement is fascinating and points up the intricacies of the possible anatomical connections involved. (Certain findings, for example, can be explained on inhibitory cerebellar function being disturbed, but others require a theoretical pathway in which there is a double chain of inhibitory function, and only by releasing the inhibition *of* the inhibition can deviations be clarified.)

The discussions on pupil and on nystagmus are still the most useful the reviewer has seen. Both chapters have been expanded and to advantage. The classification of nystagmus is superior to that usually noted in neurological texts, and allows the reader to reason on the basis of what he sees on direct examination of the patient.

It is certain that this monograph will continue to hald an eminent position in neuro-ophthalmology. It is unique, complete, and authoritative. Every ophthalmologist should have it in his working library.

Report of Meetings

NINTH ANNUAL WILLS HOSPITAL CLINICAL CONFERENCE

The Ninth Annual Clinical Conference for the Ex-Wills Residents' Society at the Wills Eye Hospital was attended by 400 ophthalmologists from all parts of the country and from overseas. The major address, the Bedell Lecture, was presented by Dr. John McLean. Dr. McLean in very succinct and clear fashion enumerated the criteria to guide decisions as to medical and surgical management in the primary glaucomas. He suggested that Stallard iridencleisis, one pillar and two pillar iridencleisis can be properly selected for the patient with glaucoma associated with narrow angles by considering the status of the angle, coefficient of aqueous outflow, appearance of the nervehead, level and status of the base pressure, and the functional ability of the eye. Dr. McLean stressed the importance of the visual field as a guide in determining the adequacy of the control of the glaucomatous process in the wide angle types. He was also impressed with the value of tonography but stressed that this must not be considered alone but only in conjunction with other findings in evaluating each eye of every patient.

He emphasized the importance of peripheral iridectomy, complete iridectomy, iridodialysis, or adequately performed iridotomy in early angle closure glaucomas. Time did not allow him to consider the complications of surgery and the problem of reoperations in glaucoma. He accented the fact that the ophthalmologist was treating a patient with glaucoma rather than a glaucomatous eye. It was a very well received and appreciated lecture that should be read by all when published.

Dr. Paul and Dr. Fry impressed the audience with the possibilities of the use of sutures to hold the retina in place. These studies revealed how well the experimental animal eye tolerated suture material when this was placed either over the retina or between the retina and choroid. The most satisfactory results were produced by 6–0 silk. Nylon produced the most severe retino-choroidal reaction and was not considered suitable for possible repair of retinal detachments. Reaction produced by silk or chromic catgut was confined to the area of the suture. The remainder of the retina did not seem to be affected.

In addition to the cases previously reported by other workers in the Wills radioisotope laboratory, Dr. Carmichael and Dr. Leopold presented 79 cases. There was a total error of 15 per cent including those lesions inaccessible to the anterior probe. It was important to note that these studies revealed that the previous criteria of a positive reading in one hour with a higher degree of positivity at 24 hours after the injection of P-32 was still applicable for lesions of the anterior portions of the choroid but that the results with iris tumors indicated that a change in interpretation was necessary. It was noted that in some eyes harboring malignant melanoma of the iris the initial reading for P-32 uptake was less than 30 per cent but that a 24-hour reading showed a rise in uptake over the 1-hour reading which in 5 out of 6 of the iris lesions studied was 30 per cent

greater than the control areas. The 6th one was 28 per cent. It is suggested by these studies that the criteria for a positive iris lesion should be a reading for 24 hours greater than the reading of one hour and this should exceed the control area by 28 per cent.

Studies by Drs. Sery, Paul, and Leopold demonstrated that novobiocin will penetrate into the intraocular tissues and fluid after subconjunctival injection of 12,500 μgm. and can be tolerated for local application to the eye in concentrations of 10,000 μgm. per cc. Penetration increased as with other antibiotics when the corneal epithelium had been removed. Massive doses were required by intravenous injection in order to produce bacteriostatic levels in the aqueous humor. Intra-aqueous and intra-vitreal injections of less than 2000 μgm. were fairly well tolerated by the experimental animal eye and remained at high levels for a minimum period of 24 hours. This antibiotic is particularly noteworthy in overcoming staphylococcus aureus and gram positive organisms resistant to other antibiotics.

Dr. Vogel's studies with the implantation of substances intralenticularly demonstrated a difference in permeability of the lens substance in the young and old lens. It is suggested by these studies that the fluorescein molecule may form a union with lens constituents as it was observed to remain intralenticularly for a period of 11 months.

Dr. Arthur Keeney discussed the importance of considering the structure of the orbit as an influencing factor in strabismus, and Dr. Kirkegeorge reviewed many of the factors which should be considered in attempting to prevent intraocular foreign body inclusions after intraocular surgery.

Dr. Edmund B. Spaeth stressed the possibility of operating on unilateral cataracts and the use of contact lenses in order to obtain binocular vision for these patients. He felt that at least 80 per cent of them could do well binocularly after operation. We may be doing these patients a disservice by asking them to wait until the second eye showed definite visual reduction. This impression confirms earlier studies presented several years ago by Drs. McLean and Constantine as well as others.

Dr. Samuel DeLong showed that the rabbit eye could tolerate an acrylic implant such as the Strampelli lens in the anterior chamber and in the discussion of this paper Dr. Brown illustrated the results in human eyes that he and Dr. Wolfgang Lieb had obtained. He also mentioned the earlier work of Strampelli and Schreck with these implants in human eyes.

Dr. Leonard Apt who has had considerable experience with tonography in infants showed the potential value of this test in aiding the control as well as diagnosis of glaucoma in this age group. He has also developed an apparently satisfactory method for anesthesia and has standardized the technique under this anesthesia.

Dr. Fairfax and Dr. Schlezinger reviewed the case of myasthenia gravis seen at the Wills Hospital. Several of these cases had had ptosis operations elsewhere before the diagnosis of myasthenia had been established. Most of the patients benefited from prostigmine, mestinon, and in some instances from ACTH ther-

apy. ACTH should only be given in "ocular" myasthenia because within 24 to 48 hours after it is given symptoms may become worse. These patients may then improve and may hold this improvement in oculomotor function for months. The ages of the patients extended from those born with the disease to those who acquired it in the late years of life.

Dr. Warren Reese presented several of his patients who were elated with their Ridley implant. As his experience has increased, his complications have decreased.

Drs. Bridges and Kaye reviewed the cases of familial dysautonomia and carefully demonstrated all the problems and difficulties of the management of these youngsters.

Dr. Bernard Gettes pointed out the necessity of taking time with patients with low visual acuity and the rewards which may occur in the occasional individual with the properly fitted and selected magnifying devices. The patient who is adequately motivated can do well with these lenses.

Drs. Paul and David Gold and Dr. Leopold presented their experience with the new potent anticholinesterase agent called phospholine iodide which appears to aid in control of many eyes with glaucoma previously uncontrolled by medical therapy.

Dr. Krewson clarified the diagnosis of oblique muscle involvement and the mechanics involved in their action.

Surgery was performed by all the attending surgeons over television and the cases included ptosis, cataracts, iridectomies, iridencleises, oblique muscle surgery, scleral resection, and vitreous implantation.

Everyone had an enjoyable time at the meeting, particularly at the libations and dinner held at the Barclay Hotel on Friday, and the Ex-Wills Resident Society had its annual meeting to close their session Saturday evening, February 9th. The exhibits were well attended; perhaps one of the unique features of the meeting was the fundus photographs demonstrated by Dr. Bedell; the diagnostic contest was won by Dr. Jim Finnegan of Creighton University.

IRVING H. LEOPOLD

Clinical Practice

Accommodation and Refraction

CHROMASIA OF THE EYE EMPLOYED AS AN AID IN THE DETERMINATION OF REFRACTION

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Klin. Monatsbl. für Augenheil., 1956, *129:* 534–543

The eye as an optical tool shows dispersion of color but as a sensory organ it is achromatic under normal conditions. Dispersion of color in the eye can be demonstrated most definitely if one uses light which is composed of 2 colors, the refractivity of which differ as much as possible. Helmholtz recommended the use of a cobalt glass for this purpose; it absorbs the rays from the center of the visible spectrum and allows only the outermost colors of the spectrum—red and purple—to pass.

The refraction of short-wave rays is stronger than that of long-wave rays. Thus focal points are produced for the corresponding areas of the spectrum. Depending on the location of the focal point with regard to the retina, the picture differs when one observes a white source of light through the cobalt glass: with myopia one sees a red disk with a blue edge, with hypermetropia one sees a blue disk with red edge. In case of astigmatism, the colored disks lose their roundness, they are distorted and assume the shape of a spindle or a rod, and a cross with a red and a blue beam is formed respectively, when the section assumes a position in the interfocal center. Many attempts were made to use this behavior as an aid in the determination of refraction. Rössler used this method in order to determine the axial position and the amount of astigmatism with the aid of the cobalt lamp. This lamp consists of a case containing an electric bulb which provides strong light, and the cobalt filter and an iris diaphragm in front to regulate the size of the light-disk. For the determination of the refraction, glasses are placed in front of the eye examined until the picture of the so-called chromatic emmetropia is offered, i.e., a reddish disk with a small blue edge. Although the method seems simple, its practical usefulness is considerably limited by the fact that the cobalt lamp produces only colored dispersed figures.

A different device is used for the "duochrome test." It consists of a lamp-case which carries two lines with black letters; the upper line has a red transparent background, the lower line, green. The duochrome test is based similarly on the principle of chromasia of the eye, but there is a fundamental difference as compared with the cobalt lamp: the black letters of the duochrome test are offered

to the eye on two different carrier waves, and the letters can be seen sharply defined only if the eye is adjusted to the focal point of the corresponding carrier wave. A myopic eye sees the letters more sharply defined in the red line, and a hypermetropic eye, in the green line; both lines appear equally clear to the emmetropic eye. The duochrome test is practically useful in confirming the spherical component of correction determined by skiascopy (retinoscopy) without using paralysis of the accommodation.

The two-color principle alone seems less suited for practical purposes in the determination of astigmatism. The author, therefore, combined the test figures which had been used by other workers, on a common rotary disk which is evenly illuminated; it shows a crossbeam in combination with a Maddox-V as it was used successfully by Lebensohn in its "astigmometer," and in addition 2 red-green squares with 2 double lines which are in an appropriate vertical position to one another. The spherical and cylindrical component of refraction can be exactly determined with the aid of this device, but it must be admitted that the two-colored test-squares are of little practical value; they are useful only for testing the "diffusion."

The duochrome method may also be used occasionally when it becomes necessary to determine whether a supplementary correction for nearsightedness may be required. An angular rod-lamp is the device used for this purpose which carries a photographic positive on glass with a small Snellen table, one in green and one in red. The optotypes are limited to the values of 20/50 to 20/15 and their size is reduced to such an extent that they are equivalent to an observation-distance of 33 cm. An emmetropic eye with good power of accommodation sees the letters on the green background more sharply defined than those on the red background, because the author uses a hypermetropic adjustment for nearsightedness. A supplementary correction for nearsightedness should be selected only to such a degree that the letters on the green table appear somewhat more sharply defined than on the red table. An overcorrection is indicated when the letters on the red background become more sharply defined. Studies with the dynamic skiascope showed that with nearsightedness the accommodation always lags behind the convergence. The assumption that 3 diopters are used for the adjustment of an emmetropic eye at a distance of 33 cm. is only conditionally right. The used accommodation is as a rule smaller, about 2.5 diopters. For the determination of supplementary near correction the two-color principle, therefore, can serve only as a control to avoid overcorrection.

Comment: One of the fundamental facts in physiologic optics is the existence of chromatic aberration in the human eye. Periodically some worker in the field becomes aware of its existence and considers its use in the determination, diagnosis, and correction of refractive errors.

While the total range of chromasia of the eye, from the just-perceptible violet to the frequencies at which the red fuses into the infrared, compass about 3.00 D. in refractive power, the refractive range with the usual red and green filters used in duochrome tests do not include more than 1.50 D. The range of the cobalt blue glass suggested by Helmholtz, and until recent years included in the standard lens test case, is somewhat more,

but this test is, of course, a crude one and has not been used practically for the determination of refraction for the last sixty or seventy years. In this day of precise refractive procedures, any use of cobalt blue lenses, cobalt filters, or any device which uses monochromatic or duochromatic light with fixation only upon a small light source is an anachronism.

Monochromatic light with frequencies corresponding to the violet end of the spectrum has been both suggested and used for subjective testing and for retinoscopy. The rationale of these procedures is that the patient, during the test, will accept greater convex lens power or less concave power, as the case may be, than he would if tested with ordinary white light with which it is supposed he would subconsciously select the middle part of the spectrum at or near the "D" line as that for which he would focus.

It is quite true that under monochromatic conditions the average patient would exhibit the expected lens power shift, but it would seem that nothing would be gained by the procedure inasmuch as in order to wear glasses comfortably, a suitable allowance would have to be made for the changes introduced by the monochromatic light source because the accommodative mechanism of the eye would be unaffected by either test. There is no virtue in getting the eye in this way to accept more convex lens power if it is necessary to reduce it an equal amount in order to afford normal vision.

The duochrome test is one which is used to a considerable extent in the United States, and one which gives satisfactory results in the hands of its devotees. In this procedure, normal "Snellen" characters are used against red and green backgrounds. Clarity of the characters is to a considerable extent dependent upon contrast factors in their surroundings, and thus a different focal value is required to see clearly the black characters on the two backgrounds. Dioptric differences of the two backgrounds will vary somewhat according to the major wave lengths of the filters used. Those commonly employed in the duochrome tests vary from 1.00 D. to 1.50 D., the average probably being about 1.25 D.

Major difficulties in employing the duochrome tests fall into two categories. The first is the subjective difficulty encountered in arriving at the judgment of equal blurs, because when the optimum test point of the duochrome procedure is reached, the Snellen characters on the red and green backgrounds are equally blurred. The second inherent difficulty is that the optimum wave length for white light is assumed to be just half way between the frequencies of the backgrounds, and this may not be true, especially in those cases where the patient's eyes are adjusted for greater sensitivity to wave lengths on either side of the "D" line, as is true in the so-called protanopic or deuteranopic individuals.

Even with these theoretic disadvantages, the duochrome test is still a useful method when its limitations are understood and allowed. However, the duochrome test does not in any way affect normal or excessive ciliary muscle tonus, and consequently presents no advantages from the standpoint of uncovering abnormal accommodative action. Cycloplegia is just as necessary with this test as it is with the tests using normal light.

There would seem to be no advantage whatever in a duochrome test for near fixation, as a much more satisfactory determination of presbyopic additions can be made by determining the range of clear vision with the proper add.

As the author of this paper points out, the duochrome test is not well adapted for the determination of ocular astigmatism. For this purpose, the Lebensohn Axometer without the colored squares would seem to be adequate as a subjective test for axis, since the addition of any chromatic test would lessen rather than increase its sensitivity.

We may expect to have other papers in which other workers will attempt to use the chromatic characteristics of the eye for the correction of refractive errors, but it is doubtful

if much that is new will emerge from these efforts. The basic problems in refraction work are those which are inherent in the innervation and responses of the ciliary and iris muscles, and these are unaffected by variations in wave lengths of incident light.

EDWIN F. TAFT

COLORED GLASSES

EDITORIAL

J. A. M. A., 1957, *163:* 264

Repeated efforts have been made to discover special virtues in tinted screens for television viewers, tinted spectacles for sunbathers, and tinted windshields for automobile drivers. Unfortunately, despite the complexity and beauty of many of the transparent colored substances made available by modern technology, many of the claims made for tinted optical products have been found to be misleading. In connection with automobile driving, especially at night, it has been shown that any colored lens impairs the driver's ability to discriminate colors. Owners of drive-in theaters discovered that supposedly glare-resistant windshields were blurring black-and-white motion pictures, making Technicolor unrecognizable, and spoiling three-dimensional effects. A campaign was therefore launched to persuade automobile manufacturers to attack the problem of glare in some other way. Tinted lenses have similarly been found to interfere with the enjoyment of television in color.

In a study of snow goggles, Wyzecki noted that safe driving or skiing in the "arctic whiteout" depends on the early recognition of cracks, holes, and humps in the snow field and reached the conclusion, after considering the possible advantages of colored over strictly neutral glasses designed to absorb uniformly over the entire visible spectrum, that "even red glasses of extreme purity . . . are not significantly more effective than neutral glasses."

Under the conditions of the arctic whiteout, a different optical principle has a curious application. It has long been known to Eskimos that an otherwise dazzling landscape of snow can be viewed comfortably by looking through pinholes in a sheet of opaque substance, and that both nearsighted and farsighted people can see things more distinctly than usual by this device. This principle has been used not only in protecting the eyes of explorers in polar regions but also in helping patients waiting for their eyeglasses after cataract operations and those who wish to read while under the temporary influence of a cycloplegic drug.

Neutral glasses, reducing the general brightness of the transmitted light without imparting to it any one color, are useful in many situations. No commercially marketed sunglass, however, is sufficiently dense to permit direct gazing at the sun. Failure to heed warnings in this respect has been responsible for many retinal burns during solar eclipses.

Red glasses are useful to roentgenologists in preparing for sessions with the fluoroscope. The continued use of enough red light for seeing, and even for reading, does not prevent dark adaptation to the rest of the spectrum. This fact is applied in the lighting of instrument panels for aircraft, on which dials illuminated with red light can be seen without impairing dark adaptation.

Although there are still certain problems to be solved in this field, an adequate factual basis now exists for answers to most of the questions patients are apt to ask their doctors. With regard to the standard sunglass listed in the Survival and Personal Equipment Officer's Manual and in the Air Force stock catalogue, the inquirer can be told that it has 15 per cent transmission over the visible range, that it looks black or gray, and that no color predominates.

The Intraocular Pressure

ON THE SURGICAL TREATMENT OF PRIMARY GLAUCOMA

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Eye Digest: Watson Gailey Foundation, 1957, *10:* 3–17

In acute glaucoma most authors believe that the eye should be operated as soon as medicinal therapy has caused the attack to subside. In chronic noninflammatory glaucoma the question of surgery is quite different. The arguments for a conservative therapy are mainly of a theoretic nature. Glaucoma is a disease which does not only affect the eye, but rather the organism as a whole, in the form of a neurovascular disorder, neurovegetative dystonia and diencephalic anomaly, so that the treatment indicated for glaucoma is not local but systemic. Also, the conservative treatment may serve to defer the operation, thus enabling the doctor to comply with the wishes of patients, who are often apprehensive.

Against conservative treatment stands the well-known fact that any kind of eyedrops will prove ineffective once the individual is habituated to the drug, eventually necessitating an increase in dosage. The effectiveness of miotics is transient, generally confined to a few hours; consequently when ointments are applied before going to bed, an increase of intraocular pressure which occurs in the early morning hours cannot always be prevented or even reduced, because of the time span. In addition, there is the psychological fact that in the course of prolonged treatment many patients become negligent in carrying out their instillations regularly, especially if instillations are to be made at frequent intervals, and if the glaucoma is of a noninflammatory type, causing no symptoms. On the other hand, with nervous and apprehensive patients, these regular instil-

lations breed an ever-mounting neurosis, because they give the patient the feeling that he is suffering from a chronic and possibly dangerous eye disease. There is, too, always the fear of a sudden attack, and—in spite of the medicinal treatment —the ever-present prospect of an operation. All of these considerations ultimately point to the fact that the "disease" glaucoma is one that no amount of eyedrops can cure.

Against surgical treatment of glaucoma we can adduce that every glaucoma operation carries certain inherent risks, which are beyond the powers of even the best surgeon to prevent. Just as a cataract operation may lead to intraocular infection and expulsive hemorrhage, there lurks behind every glaucoma operation, no matter how harmless, the spectre of *malignant glaucoma*, the probability of which can neither be prognosticated *before* it occurs, nor can this condition be treated effectively when it *does* occur.

With surgical treatment, too, is the possibility that in many cases one glaucoma operation is not enough to completely and permanently reduce intraocular pressure to normal. Even though in most cases there is no need for more than one secondary operation, there are other cases in which four to five operations are necessary before pressure is permanently relieved without the administration of miotics. And finally, what the operation cures is not the "disease" glaucoma as such, but only its principal symptom, i.e., the increased intraocular pressure. As long as we know nothing of the real nature of glaucoma, neither conservative nor surgical therapy can aim at attacking the disease by its roots, and we have to content ourselves with merely eliminating its symptoms.

For surgical treatment there is the fact that only surgery can permanently eliminate the increased pressure and its attendant risks with regard to the function of the eye and the blood vessels of the retina. With an operation successfully carried out there is no further need for continued medicinal treatment, thus freeing the patient of an enormous nervous strain. Once the pressure has been brought down to normal, there is also an improvement in the general vegetative neurosis of particularly nervous patients.

These remarks necessarily lead to the question of the most favorable time for an operation. When should a glaucoma be operated?

Personally, I am in favor of operating at an early stage for the following reasons: (1) any damage done by the chronic glaucoma to the function of the eye, i. e., visual acuity and the field of vision, is irreparable; (2) any operation for glaucoma has a better chance of success when performed in the initial stage of this condition as long as no irreparable anatomical changes have as yet taken place, particularly in the region of the chamber angle and the root of the iris (the condition of which will determine the prognosis of most glaucoma operations); (3) the later a glaucoma operation is performed, the greater is the danger of complications, such as postoperative deterioration of the field of vision and of visual acuity, abnormal hemorrhages and opacities in the lens.

However, as long as the patient's visual acuity and field of vision remain normal, and intraocular pressure can be kept below 30 mm. Hg I would never urge an operation. On the contrary, I believe that in any case a prolonged period

of observation is absolutely essential, since this is the only way to give the patient time to psychologically adapt himself to the problem of glaucoma, and thus to make him realize for himself the necessity of the operation. Half the battle is won when the patient is convinced of the necessity of the operation, and the other half depends on how early it is performed. As soon as the patient's visual acuity and field of vision begin to be affected I advocate operation. Since most patients do not consult a doctor until the function of the first eye is already impaired, the decision will be easy in these cases. As to the second eye, however, which is still fully functioning, the above principle of adhering to a prolonged period of detailed observation should be followed.

The ultimate aim of any surgical treatment of glaucoma must be to enable the patient to do without the application of miotics. If this objective is not achieved by the first operation, there must be a second. However, the second operation should not be performed too soon after the first, unless there are cogent reasons for such a procedure. The eye must first be given time to recover. Especially after fistulating glaucoma operations a suitable *massage of the eyeball*, carried out six to ten times a day for several weeks, may be successful in enabling the inadequately functioning scar to act as a fistula, thus saving the patient the necessity of a secondary operation.

At this point I would like to caution against surgical polypragmasy as well as against applying operating techniques which have not yet been sufficiently tried. This warning also applies to the extreme techniques which go under the name of "combined operation," e.g., the combination of a sclerectomy, an iridencleisis and an inverse cyclodialysis, at the same time, and the like, where an excessive operative trauma is imposed on the eye. In may many years of clinical practice I have seen a large number of cases where loss of sight was caused mainly by too short intervals between operations, or by the combination of different operations.

Up to the present, the surgical treatment of acute inflammatory glaucoma still consists for the main part in Graefe's iridectomy, which should be carried out as soon as the acute glaucoma attack has been brought to subside by the administration of miotics and Diamox (generally the day after the attack). However, the operation should not be performed at a time when intraocular pressure is higher than 50 mm. Hg since otherwise there is the risk of expulsive hemorrhage and of lens dislocation, for in Graefe's iridectomy a larger incision is made into the glaucoma-affected eye than in any other glaucoma operation, and the sudden reduction of pressure from 50 mm. Hg to zero may precipitate the complications metioned above.

The most suitable secondary operations after iridectomy are, broadly speaking, cyclodialysis and cyclodiapuncture, but the iridencleisis of a coloboma pillar will also serve the purpose well.

For chronic noninflammatory glaucoma the fistulizing operations are the method of choice today, and rightly so, for in these cases iridectomy often fails. The principal operating techniques applied are trepanation according to Elliot, sclerectomy according to LaGrange and iridencleisis according to Holth.

LaGrange and Elliot's operations produce a greater number of freely fistulating

scars than does iridencleisis. This is both an advantage and a drawback. The advantage lies in the permanent reduction of pressure, the drawback in the fact that these operations occasionally overshoot the mark, leading to hypotonia and its sequels: the development of cataracts and the risk of secondary infection in freely fistulating scars (14 per cent of secondary infections among the fistulating cases). These two facts, which were statistically evidenced by our material on glaucoma, were the reasons why I turned to iridencleisis in 1921, and have been performing this operation ever since as the method of choice and the first operation in chronic noninflammatory glaucoma.

My own technique of iridencleisis consists in incarcerating one iris pillar after performing a meridional iridotomy up to the root of the iris. I believe that it is important that no major hemorrhage occurs while the conjuctiva is cut, that none of the anterior ciliary blood vessels is injured or cauterized, and that at the end of the operation the conjunctiva is not sewn up, but that the edges are held together quite loosely and superficially by a suture which goes through only the superficial layers of the conjunctiva. Profuse bleeding of the conjunctiva and episclera, cauterization scars and an extensive suture of the conjunctiva tend to counteract the development of a loose fistula.

When the first operation fails, we generally carry out cyclodialysis according to Heine as a secondary operation, as a rule in the lower temporal quadrant. In most cases this operation is sufficient to reduce pressure to a normal level. A welcome addition to the range of secondary operations for glaucoma is cyclodiapuncture according to Vogt, as well as cyclodiathermia non perforante according to L. and R. Weekers.

To date we have mainly made use of this technique as a third or fourth operation, i.e., in glaucomas where other operations had failed and we were pleased that in a quarter of these otherwise hopeless cases we were able to normalize the pressure by means of cyclodiapuncture. After all, Vogt himself indicated this operation for glaucomas where the anterior chamber had not been restored after glaucoma operations, or for saving the eye and freeing the patient from pain when the glaucoma is a sequel of venous thrombosis. As a secondary operation it is very useful because it can be performed under conditions where the usual glaucoma operations can no longer be carried out, e.g., when the anterior chamber is absent.

Comment: This comprehensive review of the surgical treatment of glaucoma gives an excellent idea of the present Mid-European thinking in this field. The terminology of acute inflammatory and chronic noninflammatory glaucoma corresponds to the North-American angle-closure and chronic simple (open-angle) glaucoma, respectively.

Pillat's warning against combined operations is timely, since many of these operations combine procedures which are often antagonistic to one another.

H. SAUL SUGAR

GLAUCOMATOCYCLITIC CRISES

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South. M. J., 1957, *50:* 257–258

Glaucomatocyclitic crises form an interesting and homogeneous group among the various types of glaucoma that do not fall within the well-recognized primary and secondary classifications of the disease. Credit for establishing the syndrome as a clinical entity must be given to Posner and Schlossman, who in 1948 carefully studied and analyzed a series of 9 cases. According to their classification, the disease is unilateral, and although the patient may experience slight discomfort, colored haloes or blurring of vision, there is no pain and vision is usually good even at the height of the attack. The eye is white, or a few dilated conjunctival vessels may be visible. If the tension is very high, mild congestion of the sclera or edema of the corneal epithelium may be present. Ocular hypertension may appear a day or two before, or simultaneously with, cells in the aqueous, followed usually within the next 24 hours by 1 to 20 small, well-defined, unpigmented precipitates on the posterior surface of the cornea. After subsidence of the hypertension, the precipitates fade away within a few days to a month. At no time is there more than a trace of aqueous flare, and posterior synechiae are never formed.

The angles were open in four of the nine cases studied by Posner and Schlossman. The attacks of hypertension have lasted from a few hours to one month, but rarely over two weeks. Episodes may occur with varying frequency and without any apparent cause. Treatment does not seem to shorten the course of the attack, but ½ to 2 per cent pilocarpine hydrochloride may lower the tension temporarily.

Symptoms typical of the syndrome of glaucomatocyclitic crises were presented by a 41-year-old woman who had had intermittent headaches and periods of dimness of vision for one week before she was seen for the first time, in December, 1932. These symptoms began at the onset of an acute coryza. On examination, the vision in the right eye was found to be 20/20 and in the left 20/20 plus. The anterior chambers were of normal depth, there was no heterochromia, and the color and pattern of the irises were similar. The right pupil was slightly dilated and reacted sluggishly to the light. There was slight congestion of the globe but no ciliary injection. The fundi appeared normal. Slit-lamp examination of the right eye revealed 7 or 8 small white keratitic precipitates. Only a faint aqueous flare and no cells were seen. There was no synechiae. The tension was 55 mm. Hg in the right and 25 mm. Hg in the left eye. Although it was felt that the findings would justify a diagnosis of "quiet iritis with secondary glaucoma," miotics were prescribed, perhaps intuitively. A solution of pilocarpine hydrochloride, 2 per cent, and eserine sulfate, 0.5 per cent, were used locally, and the patient was admitted to the hospital for treatment and study. Two days after

admission, the tension in the right eye dropped to 30 mm. Hg and five days after admission to 26 mm. Hg. The tension in the left eye varied from 25 to 26 mm. Hg during this period. The tension in the right eye continued to remain normal and in 10 days after admission the keratitic precipitates, which had at first increased, were virtually gone.

This patient has had about 15 similar attacks involving only the right eye since her admission to the hospital in 1932. The tension during the attacks has varied from 32 to 38 mm. Hg and in each instance with one or two exceptions the attacks have begun with or shortly after an attack of acute coryza. Each attack subsided within a few days or a week without sequelae. Each responded to a weak solution of pilocarpine and more recently to pilocarpine and cortisone locally. The visual fields are essentially normal and the patient's present vision in each eye with correction is 20/20.

Little is known about the etiology of this syndrome and the problem is further complicated by the association of allergy in some of the reported cases and the probable influence of other conditions such as coryza in causing the attacks. Conservative measures should always be given a trial in the treatment of this condition. Weak solutions of pilocarpine hydrochloride and the use of cortisone locally appear to be effective in controlling the attack in most cases.

Comment: The glaucomatocyclitic crisis is indeed an interesting type of glaucoma and, from a differential diagnostic point of view, is important. It should be classified as secondary so that its relation to other uveitic glaucomas can be realized.

Although pilocarpine and cortisone locally are effective, and cortisone alone usually controls the situation quite adequately, episodes do occur in which the tension rises in spite of their use, cortisone alone or the two together. Diamox in the usual doses of 250 mg. every 6 hours for one day usually is very effective and can then be followed by cortisone. Apparently the condition occurs in episodes which fit the description of crises such as occurs with other conditions such as arthritis.

H. Saul Sugar

CHANGES OF INTRAOCULAR PRESSURE IN PATIENTS WITH PARKINSONISM.

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Ophthalmologica, 1957, *133:* 53–60

The intraocular pressure was studied in 23 patients with parkinsonism. The history of 15 of the patients revealed symptoms which were suggestive of encephalitis or masked encephalitis, such as fever with headache, meningitic manifestations, somnolence, spasms and pronounced mental changes. The clinical

manifestations of 4 additional patients suggested a postencephalitic syndrome. Of the remaining 4 patients, one had symptomatic parkinsonism resulting from traumatic encephalopathy, 2 had paralysis agitans, and 1 had arteriosclerotic parkinsonism. A low intraocular pressure was found in all 23 patients. The tension varied between 10 and 17 mm. Hg in the 15 patients with a history of encephalitis, between 11 and 15 mm. Hg in the 4 patients with a questionable postencephalitic syndrome, and between 11 and 18 mm. Hg in the remaining 4 patients. The intraocular hypotension was a characteristic constant feature in the patients with the postencephalitic type of the disease. There was no increased incidence of other ocular symptoms such as disturbances of the pupil, of convergence and of ocular movements in the patients with pronounced intraocular hypotension. No relationship between the pressure of the spinal fluid, blood pressure, and intraocular pressure could be demonstrated.

Intraocular hypotension, a new characteristic symptom of postencephalitic parkinsonism, is considered the result of a postencephalitic degenerative process in the diencephalon which causes a functional disturbance of the centers which control the intraocular pressure. It seems likely that a functional disturbance of the cortico-striato-thalamo-hypothalamic tracts may also play a part.

Comment: The observations of Brand should direct the reader to corroborate or disprove their important implications. If they can be corroborated, they will add further to the evidence that a cerebral center exists which controls intraocular pressure. One must be careful in evaluating tension in parkinsonism, depending on the effect of the disease on the orbicularis. In cases of parkinsonian blepharospasm there would be a tendency to find a false elevation of pressure while in those where a decrease in muscular tonus is present, low ocular tension would be found.

H. Saul Sugar

THE AMORPHOUS SUBSTANCE IN THE TRABECULAR MESHWORK

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Brit. J. Ophth., 1957, *41:* 20–24

Virchow, in his description of the microanatomy of the trabecular meshwork, mentioned the presence of some unfamiliar tissue-element in addition to the known structures. In the trabecular meshwork of the horse, he observed fine threads originating and terminating in the endothelial cells, and running through the empty spaces of the meshwork. So far as known, no other description of this substance appears in later reports on the morphology of the trabecular system.

In working on the problem of the innervation of the trabecular meshwork a similar picture has very often been seen by the author. As his sections were mainly cut on the freezing microtome, the tissue components were better preserved than they are in paraffin sections. In flat preparations of the trabecular meshwork, thin sheets of a perfectly transparent substance were often seen. Their existence was indicated only by the presence of silver deposits. Even in frozen sections, however, it was not possible to explore this substance in detail, because it was not found in meridional sections. A systematic search was therefore made for a better method of embedding. Paraffin infiltration causes great deformation and celloidin was also found to be injurious to this delicate tissue component. Many other methods were tested with little success. Eventually, however, Celodal-embedding was tried at the suggestion of J. Wolf of Prague. This procedure causes only minimal changes in the amorphous substance, but once it is polymerized the Celodal cannot be removed from the sections by any solvent. In addition, the Celodal itself takes up some color.

Study of sections obtained from sheep's eyes, embedded in Celodal, and stained with cresyl violet showed that all the spaces between the trabeculae were apparently filled by an amorphous substance staining a reddish violet. In the meshes of the uveal trabeculae no appreciable amount of this substance was found. Although the substance did unquestionably stain metachromatically, its color was quite different from the very reddish metachromasia of the corneal stroma. The collagen bundles of the sclera stained faintly pink, but the trabeculae appeared unstained by contrast, probably, with the compact colored substance. The ciliary muscle following the trabecular meshwork took on an intensive, more bluish tone. The endothelial cells were practically invisible against the great amount of amorphous substance, but in thin sections or in older preparations, they could be seen as a very thin, darkly colored lining of the colorless trabeculae. When the Celodal sections and paraffin sections stained with cresyl violet and mounted in glycerol gelatin were compared, it was found that after embedding in paraffin a considerable shrinkage of the amorphous substance takes place, resulting in the formation of empty spaces. The endothelial cells remain close to the trabeculae, and only very fine threads run between the distorted layers of tissue. The concentration of amorphous substance is highest at the tip of the trabecular meshwork close to the cornea. The next highest concentration is in the external layers of the meshwork close to the inner surface of the sclera. The innermost layer of scleral trabeculae come next, and the middle layers of the meshwork are the palest.

The metachromatic material can also be seen in nonembedded preparations. On staining (with a 1:1000 solution of toluidin blue in water) a very thin, teased-out strip of the scleral meshwork of the formol-fixed cow's eye, a very distinct metachromasia of the meshwork can be seen.

This anatomical demonstration of the existence of an amorphous substance in the spaces of the trabecular meshwork confirms the physiological evidence provided by the work of Bárány (1956). Metachromatic staining of the human trabecular meshwork has also been seen by Persson (1954) and by Berggren

(1956), but these authors were not able to study the actual location of the metachromatic material because they used only the standard embedding media.

Comment: This study indicating the existence of an amorphous substance in the trabecular meshwork of sheep certainly may fit in with the belief of Bárány that a polysaccharide substance containing hyaluronic acid is present within the trabecular spaces but it does not confirm this, nor does the study indicate the nature and mechanism of its activity. Much remains to be learned in this regard.

This reviewer recalls Dr. L. Zimmerman's sections of the trabeculum which stain differently from the remaining tissues and looks forward to the publication of his material.

H. Saul Sugar

The Ocular Muscles

ELECTROMYOGRAPHY—A TOOL IN OCULAR AND NEUROLOGIC DIAGNOSIS

I. Myasthenia Gravis

II. Muscle Palsies

A.M.A. Arch. Ophth. 1957, *57:* 161–175

ELECTROMYOGRAPHIC EVIDENCE FOR OCULAR MUSCLE PROPRIOCEPTION IN MAN

A.M.A. Arch. Ophth., 1957, *57:* 176–180

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Electromyography requires the insertion of fine-gauge concentric electrodes through the conjunctiva directly into the extraocular muscles. The only complication is an occasional subconjunctival hemorrhage of brief duration. The muscle potentials are amplified, displayed on a dual beam oscilloscope and recorded photographically on a moving film.

MYASTHENIA GRAVIS

Involvement of the extraocular muscles may be one of the earliest signs of myasthenia gravis. Improvement in the motility of paretic ocular muscles which follows the use of anticholinesterase or anticurare type drugs may be so

minimal as to escape detection. However, electromyography reveals a striking and characteristic muscle response even though gross improvement of motility may not be evident.

In testing for myasthenia gravis, Tensilon chloride is administered to adults in a dosage of 0.2 cc. (2 mg.) intravenously over 15 sec. If there is no response in 30 sec., 0.8 cc. (8 mg.) more is administered. In one patient with ptosis and inability to turn the eyes to the right, electromyography indicated that the levator was firing only a single unit on maximum effort to elevate the lid. Thirty seconds after the intravenous injection of 1.0 cc. (10 mg.) of Tensilon chloride the muscle fired profusely although not as much as normal. The discharge gradually decreased to the earlier baseline.

There have been no responses of the above type in nonmyasthenic palsies or progressive nuclear ophthalmoplegia or in the normal subject, although it has been reported that Tensilon may cause a mild, transient increase of strength in the normal and in some nonmyasthenic diseased muscle. A patient with neurogenic ptosis and a partial third nerve palsy developed sustained fibrillations and fasciculations (10 to 15 min.) of the levator following Tensilon injection. The electromyographic tracing of this response was entirely different from that seen in myasthenia gravis and was not related to voluntary attempts to move the affected muscles.

A progressive decrease in amplitude of motor units on sustained effort, such as has been described for peripheral muscle in myasthenia gravis, has not been noted in the extraocular muscles. It is probable that anatomic and pharmacologic uniformity of the muscle fibers and the small innervation ratio result in simultaneous, total exclusion of all the muscle fibers of a unit—hence loss of the complete unit—rather than in a unit of decreased amplitude due to inactivation of individual muscle fibers.

MUSCLE PALSIES

Electromyography permits the determination of lower motor neuron denervation which is characterized by fibrillation—the minute spontaneous discharge of single muscle fiber potentials. Such fibrillations have been noted in ocular muscle palsies but caution is required in the interpretation of ocular muscle potentials because small, single motor units resemble fibrillations. Where volitional potentials are present the diagnosis must be restricted to the spontaneous potentials occurring when the eye is turned away from the field of the affected muscle. The electromyographic pattern of mild palsies cannot be distinguished from the normal.

A number of typical examples of the electromyogram in types of muscle palsy are reported. The obicularis oculi muscle recovering from Bell's palsy showed fibrillations and normal motor units with gradual disappearance of the abnormal waves as clinical improvement progressed. In pseudoparesis of muscles, electromyography indicated the normal characteristic of the involved muscle. In Duane's retraction syndrome the lateral rectus muscle showed practically no innervation while the medial rectus and levator were normal. Aberrant third

nerve regeneration which follows oculomotor nerve palsy is characterized by retraction of the upper lid, adduction of the globe and miosis on attempts to look up, down or in. Electromyography indicated that the disease resulted from random misdirection of regenerating nerve fibers so that all components of the nerve were distributed to all the muscles innervated. In progressive nuclear ophthalmoplegia the electromyogram indicated that the disease may be of muscular rather than innervational origin.

OCULAR MUSCLE PROPRIOCEPTION

The question of extraocular muscle proprioception, i.e., the awareness of the position of the eyes due to messages from the ocular muscles (as advocated by Sherrington), has now been generally denied. The information derived from vision and the innervational urge are said to be adequate to explain awareness or lack of awareness of eye position. That the extraocular muscles should lack a mechanism for the recording of muscle tension, however, would place them far apart from other skeletal muscles.

The existence of unusual nerve endings in these muscles has been reported, and the occurrence of muscle spindles and other low-threshold stretch receptors has been clearly described. Typical stretch discharges in afferent fibers running in the third, fourth, and sixth nerves, via the fifth nerve and in the brain stem, have been recorded and provide clear neurophysiologic evidence for the existence of a tension-recording apparatus in extraocular muscles.

It has long been known that stretch reflexes cannot be obtained from extraocular muscles. Electromyography was carried out during enucleation procedures under local anesthesia. The level of anesthesia was sufficiently light to permit muscle movement without discomfort. The level of firing of extraocular muscle which is characteristically seen in the primary position decreased radically when the muscle tendon was cut from the globe. Some firing continued when fascia supported the muscle and prevented complete retraction into equilibrium position. After enucleation, in another case, when the ocular muscles were maximally retracted there was no discharge in the resting rectus muscles. They now resembled typical peripheral skeletal muscle at rest. On attempted gaze to the side, however, they promptly fired. The only thing changed was the degree of stretch of the muscle. It is inferred, therefore, that the normal firing of the primary position is a consequence of a certain degree of tension in the attached muscle. Retraction of the free muscle disburdens the spindle mechanism, which ceases its discharge and thus inhibits motor unit firing. The attempt to augment motor discharge above the level found just before cutting the tendon by stretching the cut muscle was unsuccessful.

Comment: The three papers by Breinin will do a great deal to familiarize ophthalmologists with the contributions of electromyography to ophthalmic neurology. Of course, neither the technique nor the necessary instrumentarium seem to be such as ever to permit electromyography to become a tool of every day practice. It is good to know that by this technique one can better and more objectively diagnose the transient improvement of myasthenia gravis by Tensilon. So far, this reviewer could seldom convince himself

that the subjective and objective improvement reported by patients and doctors was free from wishful self-suggestion. In palsies of extraocular muscles, electromyography helps to establish the site and the characteristic of the lesion and thus one can hope that in unclear cases a better diagnosis and prognosis can be secured with the help of this method. Some examples offer encouraging results. One of the most interesting of them refers to so-called progressive nuclear ophthalmoplegia. Breinin's observations suggest that this disease entity is more closely related to muscle pathology than to a neurologic involvement.

The most interesting, at least for this reviewer, are the results of Breinin's study regarding ocular muscular proprioception. Since Cooper, Daniel and Whitteridge (Brain, 1955, *78:* 564) have finally established the presence of muscle spindles in the extraocular muscles, this problem has become important once again. Breinin makes it quite clear that what he refers to as ocular muscular proprioception does not necessarily involve the awareness of position. What he actually refers to, and what he found definitely to be present in the extraocular muscles, is the "negative feed-back mechanism controlling motor discharge, predicated on a reflex arc whose afferent end-organs are muscle spindles." The extraocular muscles have a tension recording apparatus and we can be sure it is for some good purpose. The apparatus is certainly of significance for the proper adjustment and coordination of the extraocular muscles, that of positioning the globe. Whether proprioception has anything to do with space perception is of course, another question.

ARTHUR LINKSZ

MARCUS GUNN PHENOMENON FOLLOWING SQUINT AND PTOSIS SURGERY

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Vancouver, British Columbia, Canada

Pacific Coast Oto-Ophth. Soc., 1956, *37:* 91–100

The Marcus Gunn phenomenon, which is often inaccurately referred to as the jaw-winking phenomenon, appears in typical cases as a unilateral congenital ptosis in which there is a retraction of the lid on opening the jaw; this startling associated movement is usually obvious on sucking in infancy. Variations in this picture are sometimes found: thus in rare cases the phenomenon may be bilateral. Its development in later life as a result of trauma or even without apparent cause has also been reported. Occasionally it seems to be inherited, and in some cases it has been found in association with other deformities in addition to ptosis, e.g., paralysis of the superior rectus or the internal rectus, or external ophthalmoplegia, facial asymmetry, nystagmus, and seesaw movements of the lids. In the subject of the present report, palsy of the superior rectus and some facial asymmetry were associated with a unilateral congenital ptosis.

The stimulus to lid retraction may be provided by various movements of the jaw or of the eyes.

Abnormal nervous connections are believed by most authorities to be the cause of the Marcus Gunn phenomenon, but the location of the aberrant connections is by no means unanimously agreed upon. Some authors believe them to be cortical or subcortical, others think the fault lies in the internuclear connections, and still others blame defects in the infranuclear connections. A physiological explanation for the phenomenon, on the other hand, is regarded as more acceptable by Duke-Elder, and Wartenberg (1946) lists three neurophysiologic principles as worthy of consideration, i.e., (1) irritation of normally dormant connections, (2) release of inhibition, and (3) spread of impulses by irradiation. The interesting suggestion that the cause of the phenomenon, which sometimes resembles the primitive gill, mouth, and eye opening reflexes in fish, is a release or an irritation of an ancient phylogenetic reflex (first proposed by Harman in 1903) is supported by several notable authorities.

None of these explanations, however, holds true in the present case in which the jaw-winking phenomenon appeared after the surgical correction of ptosis in a 28-year-old woman. The patient, an otherwise attractice office worker, requested improvement in her appearance. She had had a left ptosis since birth, associated with a downward and outward deviation of the left eye, which had always had defective vision. No jaw-winking had been noticed in infancy or later. No other member of the family was affected. Surgical correction was carried out in three stages: (1) left resection of the internal rectus muscle and tenotomy of the left external rectus; (2) resection, 3 months later, of the superior rectus and recession of the inferior rectus on the left side; and (3) shortening, 2 months later, of the levator tendon by a Blaskowicz type of operation. Photographs taken before operation and between the stages gave no hint of a Marcus Gunn phenomenon. The cosmetic result of the squint and ptosis surgery was good, but an obvious lid retraction was seen when the jaw was opened quickly. Deviation of the jaw to the opposite side produced a slight retraction. The movement was best concealed by bending the head down and looking up, thus placing the lid in an elevated position so that further retraction was slight and concealed by the eyebrows. The patient is proficient at concealing the lid movements, and surgical correction of the Marcus Gunn phenomenon in this case does not seem to be warranted.

The ptosis operation could not have caused abnormal nervous connections, or functional interference with reflexes, or the release of an atavistic reflex. If the phenomenon was latent before the ptosis surgery, it was certainly very well masked, as shown by the fact that it was not mentioned in the history, or revealed in any of the many photographic studies, or discovered during adequate preoperative and orthoptic examination.

Comment: The postoperative photographs certainly reveal a classical Marcus Gunn phenomenon. The commonly accepted explanation for this phenomenon is an abnormal nerve connection in the central nervous system between the nerve supply of the levator and the external pterygoids. If Dr. Derek Simpson's observations are correct this explanation does not hold, and we must search for others.

PHILIP KNAPP

POSTERIOR CONICAL CORNEA

H. B. Jacobs

London, England

Brit. J. Ophth., 1957, *41:* 31–39.

Since posterior conical cornea was first described, only a handful of cases has been added to the literature. The name suggests that the condition has some relationship with the better known conical cornea. However, there is no evident relationship beyond the unsubstantiated statement that the posterior form is a precursor of the ordinary form. The two conditions are so named merely because the cornea tends to become cone shaped—throughout its thickness in ordinary keratoconus and solely in its posterior surface in keratoconus posticus. Two forms of the latter condition occur: (1) Localized—keratoconus posticus circumscriptus; (2) Generalized—keratoconus posticus totalis.

Seven cases of keratoconus posticus circumscriptus have been recorded previously. In each instance the author described a localized concavity of varying size in a part of the back of the cornea. Six of the patients had either a localized nebula or haze. One had a definite history of trauma and another apparently had acquired the lesion. Six of the patients were men; the seventh, a Negress. Five lesions were unilateral, one bilateral, one was in an only eye, and only one was associated with other possibly relevant ocular pathology. This took the form of definite lens changes in line with the corneal lesion, which brought forth the consideration that the corneal lesion was congenital. In this paper the author describes nine additional cases. Two are father and son.

Only three cases of keratoconus posticus totalis have been mentioned previously in the literature. All three seen were in women who had had impaired vision for many years, and in all, the condition was probably congenital. One author remarked on the resemblance of the shape to that of the developing cornea. In each instance there was noted a uniform increase of the posterior corneal curvature. Two cases were unilateral; one, bilateral. The author describes one additional case. This, too, was in a woman with long standing deficient vision in one eye.

Although little is known of the possible mechanism of formations of keratoconus posticus circumscriptus, it is known that disturbance of Descemet's membrane and/or the corneal endothelium can give rise to opacities in the more anterior levels of the substantia propia. It would seem possible that such a disturbance in the very young could be accompanied either by a resorption of the deeper lamellae or failure in their formation, either of which might result in the formation of a localized posterior concavity.

The lesion of Descemet's membrane or the endothelium might take the form of a definite tear, some similar but subclinical loss of continuity, or merely a disorder of normal function of the endothelium in preserving the physiological status of the substantia propia.

The mechanism is consistent with prenatal or neonatal trauma or inflammation being responsible for the condition. Other possibilities include a failure in the normal development of either Descemet's membrane, the endothelium, or the substantia propia as a causative factor.

The author considers seven of his cases to be congenital. Insufficient evidence is available to reach a conclusion in the other two. Three cases collected from the literature were probably of congenital origin and two possibly traumatic.

All the cases presented of keratoconus posticus totalis have a long history. All had had poor sight for as many years as they could remember. The visual loss was apparently not progressive and could not be corrected with spectacle lenses. This makes it appear likely that all are amblyopic and argues for the congenital origin of the lesion.

The only bilateral case report noted a Hudson's line and a few Hassall Henle bodies peripherally. One other case report mentions a central corneal haze and pigment deposits on the posterior corneal surface.

In the present case there was a definite faint haze, and the anterior corneal surface was slightly irregular as judged on the keratometer and with Placido's disc. No other author has described both of these findings and Harrison Butler (Brit. J. Ophth., 1932, *16:* 33) states that in his case the reflections of the Placido's disc were regular. It is suggested that in nearly all cases the condition of keratoconus posticus originates in early life and is probably present at birth.

Comment: By reviewing the literature on posterior conical cornea, and adding cases of his own, Jacobs has focused attention on this condition and will assist others to classify corneal affections of this type.

It is difficult to believe that posterior conical cornea is as rare a condition as the literature would indicate. It is more likely that few individuals have seen or recognized a sufficient number of cases to warrant reporting them in the literature.

In the two cases, father and son, (cases 8 and 9) in whom the familial etiology is undoubted, all the criteria of a familial disease seem to be fulfilled. In others, the lack of bilateral involvement and the nature of the corneal scar suggest that the disease has been acquired, possibly due to inflammation in utero with localized effects upon Descemet's membrane and the posterior lamellae.

HUGH L. ORMSBY

IRIN, A SMOOTH MUSCLE CONTRACTING SUBSTANCE PRESENT IN RABBIT IRIS

J. Physiol., 1955, *129:* 651–661.

TRIGEMINOMIMETIC ACTION OF IRIS EXTRACTS IN RABBITS

J. Physiol., 1956, *132:* 491–501

PROPERTIES OF IRIN, A PHYSIOLOGIC CONSTITUENT OF THE RABBIT'S IRIS

J. Physiol., 1957, *135:* 114–135

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In rabbits, mechanical stimulation of the trigeminal nerve, or of the iris itself, causes an intense, long-lasting pupillary constriction which is not prevented by local or systemic application of atropine.

The author assumed that the sphincter spasm could be caused by a smooth muscle stimulating substance, released from the trigeminal nerve when stimulated antidromically, or in response to local injury of the iris.

Iris extracts were made from the eyes of mixed stock rabbits (including albino). With the animals anesthetized by ethyl chloride, the eyes were enucleated. The globe was opened equatorially and the iris excised and dried between filter paper.

Watery iris extracts were found to contain a pharmacologically active substance which was named *irin*. It was purified by treating the watery extracts with 20 vol. of acetone and re-extracting the acetone-soluble, dried fraction with chloroform. It could be further purified electrophoretically, behaving as a weak acid on paper electrophoresis as well as in chloroform-water partition. Irin dosage is expressed in terms of "milligram equivalents" of the original iris tissue.

Intraocular injections of such extracts induced prolonged, atropine-resistant miosis in rabbits and cats, mimicking the antidromic effect of trigeminal stimulation. *In vitro*, it was found to contract guinea-pig and rabbit ilea, the isolated ox sphincter pupillae and the histamine-insensitive diagonally striated portion of the rat's colon. The two latter preparations were found to be the most sensitive, being capable of detecting the activity corresponding to the equivalent of 0.25–1.0 mg. of iris tissue.

In an extensive series of tests, irin was proven to be a substance distinct from various naturally occurring pharmacologically active substances such as 1) cho-

line esters, 2) urochanylcholine (murexine), 3) 5-hydroxytryptamine, 4) histamine, 5) bradykinin and 6) substance P.

A substance similar to irin was found a) in the conjunctiva and b) in the aqueous humor of rabbits after paracenthesis.

Comment: In order to do justice to the importance of this interesting work, the history of this problem has to be considered. (The historical outline was prepared by Dr. I. E. Loewenfeld in this laboratory. It will appear within the framework of an extensive monograph on "Mechanisms of Pupillary Reflex Dilatation.")

In 1824, Magendie cut the 5th nerve intracranially in a rabbit. A few seconds after the nerve was cut, the pupil on the side of the lesion began to contract. The contraction movement differed from the one seen after stimulation of the third nerve. It was extensive but much slower, taking several minutes to reach its peak and, in contrast to the short duration of the contraction which follows third nerve stimulation, it lasted from ½ to 2 hours. Simultaneously, vascular changes appeared in the homolateral eye and face. Some time later, the cornea clouded and ulcerated and after a few days, the entire eye was destroyed.

Mainly because of these "trophic" changes, the effect of 5th nerve lesions attracted widespread attention, and many experiments were performed (cf. Table). As to the pupillary behavior, the following facts were established:

Miosis was produced in rabbits and in frogs, but not in man, monkeys, cats, dogs and birds, by cutting the 5th nerve central or peripheral to the Gasserian ganglion, or by damaging the ganglion itself. Miosis also developed when the descending spinal trigeminal tract was injured in the medulla or at a level as far down as the second segment of the cervical cord. Mechanical or electrical stimulation of the 5th nerve or of its peripheral stump caused the same slow, intense, and relatively long-lasting miosis. After the 2nd, 3rd, 4th or 6th cranial nerves or the cervical sympathetic chain had been cut, the phenomenon could still be elicited; similarly, removal of the ciliary ganglion and local or intravenous administration of atropine did not prevent it.

It became clear, then, that the miosis which develops in rabbits after injury or stimulation of the 5th nerve has nothing in common with any known pupillary reflex motion. Its dynamics differ from those of normal pupillary movements by the slow onset and long duration. Since miosis fails to develop when the *central* stump of the cut 5th nerve is stimulated but persists when the *peripheral* stump is stimulated and after all other nerves to the eye have been divided, it cannot be a reflex response but must be produced by an antidromic mechanism contained in the 5th nerve itself. This mechanism must be irritative in nature, because the miosis is temporary and the original pupillary diameter is regained within hours, and also, because it is elicited by stimulation as well as by injury to the fifth nerve. It is not likely to be due to vascular events, because it can be elicited in rabbits freshly killed by bleeding. It cannot be cholinergic because it persists after atropine and finally, it cannot be due to loss of sympathetic innervation because of its great extent and temporary nature and because of its persistence after sympathectomy.

Although, therefore, the extensive work done on this subject furnished much information on what this phenomenon can *not* be, its true mechanism has remained unknown up to the present.

We are delighted to see that, after about 75 years of inconclusive debate and a following half-century of near-neglect, this problem is now being attacked in a fundamentally new manner by making use of modern biochemical techniques and knowledge.

The importance of this work is possibly much greater than it seems at first glance.

Year	Author	Year	Author
1824	Magendie	1867	Schiff (frog)
1825	Desmoulins	1868	Schur
1828	Mayo (birds)	1869	von Arlt, Jr.
1834	Fario	1869	Edes
1839	Constatt	1872	Kondracki
1939	Valentin	1875	Gradle
1842	Longet	1875	Grünhagen & Samkowsky
1846	Hall	1875	Senftleben
1847	Fr. Meyer (frog)	1875	Vulpian
1851	Waller & Budge	1878	Argyropolous
1852	Budge	1878	Francois-Franck
1853	De Ruyter	1879	S. Mayer
1854	von Graefe	1884	Gudden
1854	Vulpian & Phillipeaux	1885	Neglinski
1855	Budge	1886	Schipolow (frog)
1855	Schiff	1886	Jessop
1857	von Graefe	1892	Eckhard
1858	Snellen	1892	Grünhagen
1858	Schiff	1893	Spalitta
1858	Cl. Bernard	1893	Braunstein
1860	Samuel	1900	Angelucci
1862	Balogh	1904	Levinsohn
1862	Oehl	1904	Bach & Meyer
1864	Donders	1905	Bach & Meyer
1864	Grünhagen	1908	Bach
1864	Guttmann (frog)	1921	Winkler
1864	Rosenthal	1924	Papilian & Conceanu
1866	Grünhagen	1926	Magitot & Bailliart
1867	Grünhagen	1931	Imachi
1867	Rogow	1940	Lebedinsky & Zimkin
1867	Salkowsky	1953	Maurice

As far as the pupillary reactions are concerned, the phenomenon could be dismissed as a peculiarity, restricted to rabbits and frogs, and unrelated to normal pupillary innervation. But the pupillary phenomenon was accompanied by destructive changes in the cornea and by deterioration of the globe, and these reactions, not the pupillary signs alone, elicited the interest of so many investigators through such a long period of time.

We therefore hope that the author will continue his promising research and widen its scope to an investigation of possible physiologic (or pathologic) effects of irin on the eye beyond its stimulating influence on the pupillary sphincter.

In our opinion, it appears unlikely that true qualitative differences should exist between rabbits and other species. In spite of the facts that 1) miosis due to 5th nerve damage or stimulation was not found in other mammals examined and 2) clinical reports on trophic damage to the eye caused by trigeminal conditions are not conclusive, we are inclined to believe that we are probably dealing with mere quantitative differences, either in terms of production or of sensitivity to the substance. The facts that 1) the pupil in clinical cases of iritis is often tightly constricted and fails to dilate to atropin, 2) the pupil usually becomes small when the isolated dog or cat iris is placed in warm Ringer's

solution and 3) purified extracts of rabbit iris were found by the author to affect the iris of the cat and the ox, appear to bear out this assumption. We therefore hope that future work will include investigations on this mechanism in other species.

OTTO LOWENSTEIN

The Orbit

THE USE OF RADIOGRAPHIC CONTRAST MEDIA IN DIAGNOSING ORBITAL TUMORS

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Acta ophth., 1956, *34:* 355–366

The methods of investigation available in cases of unilateral exophthalmos often prove to be insufficient to establish the diagnosis. This is probably true of the radiologic examination which in most cases fails to contribute to the proper diagnosis whether ordinary x-rays of the orbits are taken or tomography used. Visualization of the tumor in the roentgenogram permits exact localization of the tumor and an estimate of its origin. An impression of its nature is obtained by noting whether it is well defined or whether the surrounding tissues are infiltrated. Where a well defined tumor is seen, the possibility of a pseudotumor of the orbit can undoubtedly be excluded in most cases. With such information it is easier in the individual cases to decide on the form of therapy and it is especially easier to decide whether the tumor can be removed from the orbit, or whether the case is better suited for a transcranial operation.

There are three methods of visualizing the contents of the orbit in radiographs: The orbital vessels can be visualized by arteriography. A contrast medium can be injected into the veins of the orbit, and, finally, the contrast medium can be injected directly into the orbital tissues and make the various structures visible when it settles on their surface.

Carotid angiography has become well established among the neurosurgeon's diagnostic aids. It is of great importance to the ophthalmologist in cases where the diagnosis may be either a purely orbital process or one which also spreads intracranially. In practice, meningioma of the sphenoidal wing affords the best example. In such a case there will often be unilateral exophthalmos, impairment of vision and irregular contraction of the field of vision as the first symptoms; these might well be due to a purely intraorbital affection, but arteriography reveals the presence of a tumor which must be dealt with by the neurosurgeon. In most

cases of purely orbital tumors, arteriography is of less value. Vessels of orbital tumors are less frequently filled than intracranial vessels. Placement of the ophthalmic artery and its ramifications, or of the orbital veins, is seldom demonstrated because of the difficulty in obtaining satisfactory filling of the vessels and because the dense, bony structures surrounding the orbit render the interpretation of the radiographs difficult.

Orbital phlebography was first described in 1951. The orbital veins are filled with contrast medium through an injection made into the angular vein, and at the same time radiographs are taken in the anteroposterior and lateral views. In most cases the contrast media can be injected percutaneously with slight local anesthesia, but not infrequently the vein must be exposed through a small incision.

Good filling of the orbital veins, especially the superior ophthalmic vein, can be obtained with this method; this vein forms a direct connection between the angular vein and the cavernous sinus, but also the rest of the venous plexus of the orbit and the inferior ophthalmic vein can be filled with contrast medium by this route. The outflow from the orbital veins takes place through the communications with the facial veins but also through the orbital fissure inferior to the pterygoid venous plexus and through the orbital fissure superior to the cavernous sinus. In processes occupying space in the orbit this technique shows that the veins have been displaced from the area occupied by the tumor. If the tumor is in the upper part of the orbit, it can be seen that the venous outflow from this part is interrupted. The veins are thicker than normal and the outflow through the inferior orbital fissure to the pterygoid venous plexus is therefore greater.

A special indication for orbital phlebography is those cases where a venous angioma in the orbit is suspected and in those where the diagnosis of hemangioma has been established but where it is desired to ascertain its extent before the patient is operated. No complications in orbital phlebography have been reported. The patient may be hypersensitive to the contrast medium which it is intended to use; therefore, a sensitivity test should be made.

The third method of examination is the injection of contrasting agents directly into the orbital tissues. Contrast media or air may be used. The technique of air injection is quite simple. The only instruments required are sterile 10 to 20 cc. syringes and needles as used for retrobulbar anesthesia. Tenon's capsule can be filled through a curved needle inserted through the superior temporal quadrant. The muscle cone may be filled by inserting the needle through the lower eye lid as is done in retrobulbar anesthesia injections. For anesthesia only cocainization of the conjunctiva and a small local infiltration of the skin of the lower eye lid is used. The amount of air insufflated will vary with individual cases. To fill the capsule of Tenon, 5 or 6 cc. will be suitable. Outside the capsule, 10 to 15 cc. will generally be enough, but other authors have used over 30 cc.

Insufflation of air does not cause severe pain. During the injection the patient has the sensation of pressure behind the eye but this ceases as soon as the injection is completed. The air causes the exophthalmos to increase by 2 or 3 mm.

and the intraocular pressure by 8 to 10 mm. Hg. Air is resorbed from the orbit in 2 or 3 days while oxygen is resorbed in 4 or 5 hr.

Contrast media have an advantage compared to air of producing better shadows. The exophthalmos, however, persists for 2 or 3 days and pain is so marked that retrobulbar anesthesia must be used. The contrast media does not spread as easily as air so that it must be injected from more than one quadrant.

Information may be obtained by means of orbital phlebography and pneumography which cannot be obtained in any other way. In many cases these techniques may replace carotid angiography which is seldom contributory in purely orbital tumors and is a more dangerous procedure.

Comment: This article reflects the increased interest in the use of radiographic contrast media as an aid to the diagnosis of space occupying lesions in the orbit. Ophthalmologists who are particularly interested in orbital lesions are always on the lookout for methods and procedures that will make the diagnosis of retrobulbar masses easier. In this article the author approached the subject from three standpoints, i.e., orbital angiography, orbital phlebography, and the injection of contrast material directly into the soft tissues of the orbit.

The author feels that carotid angiography is a useful tool in the diagnosis of such lesions as a meningioma of the sphenoid ridge. In my own experience I would believe it possible to make a likely diagnosis of a meningioma in such a location by other means and avoid the use of carotid angiography. The risks and dangers of carotid angiography are such that I would not utilize this diagnostic procedure except in vascular lesions involving the posterior orbit. In the latter situation angiography will be of help in determining the intracranial extension of such a lesion and help the surgeon plan an appropriate attack for trapping or excision of the vascular defect. Even in this situation the advantages to be gained from such angiography must be balanced against the possible intracranial complications of the test.

In this editor's opinion the method of orbital phlebography that the author describes offers as much practical information as does carotid angiography and can be performed with much less risk to the patient. Here again, I would limit the phlebography to those situations where a vascular neoplasm or vascular anomaly is suspected. In all other situations involving an orbital mass the pattern of venous distribution and displacement would be too irregular as to offer a dependable diagnostic clue.

As a contrast media for direct injection into the orbital tissues, the author recommends the insufflation of air. Of all the contrast media that have been recommended for injection into the orbit, air seems to be the safest. As the author describes the procedure, the technique seems simple, and the patient is not unduly disturbed by the insufflation. However, for those readers who may be inclined to try such a procedure the article by Keskey and Letsch (A.M.A. Arch. Ophth., 1956, *56:* 248), is recommended. The latter authors point out some of the difficulties in making the air injection as well as mentioning some of the disadvantages to the patient (analgesia and hospitalization).

Although I have had no actual experience with the insufflation of air into the orbit, I have seen several patients on whom the procedure was done elsewhere. In these people the initial injection had been so painful that they specifically asked that it not be repeated, and in each case the information gained had not proved to be of any greater value than the information gained by the more routine inspection and palpation of the orbit. Therefore at this stage of development I would not recommend this procedure for routine office use.

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SOME PROBLEMS IN RELATION TO RETINAL DETACHMENT

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Eye Digest: Watson Gailey Foundation, 1957, *10:* 18–24

Although some thirty years have elapsed since Gonin first clarified the basic principles underlying the surgical treatment of retinal detachments, they remain the same: first, to find and localize all the breaks in the continuity of the retina, and then to close these holes and secure reapposition of retina and choroid by the removal of subretinal fluid. The many problems that still exist concern not the principles or the objectives, but rather the means of attaining them.

Efforts to discover and localize retinal tears have passed through an almost complete cycle, from the indirect ophthalmoscopy (originally advocated by Gonin) to direct ophthalmoscopy, which has been favored in the United States but which has its limitations, and back again to the indirect approach, which has been greatly improved by Schepens' addition of stereoscopic visualization, the rediscovery of scleral depression for viewing the most peripherally placed lesions, and exact localization under ophthalmoscopic observation during the surgical procedure. The advantages of stereoscopic indirect ophthalmoscopy with scleral depression are so obvious that when the limits and range of direct ophthalmoscopy, indirect ophthalmoscopy alone, and indirect ophthalmoscopy with scleral depression are compared the solution of the first problem in detachment work seems to be for every ophthalmologist to develop proficiency in this method.

The second major objective, closure of the holes, is of course dependent on the first. Every conceivable method of repair of tissue has been attempted, from direct suturing to indirect closure from inflammatory repair. Methods used for the production of sterile inflammation have included irritation from direct heat produced by the actual cautery, electric cautery, and thermophore; cold by cryotherapy; chemical insult; various types of irritation by electric current; and even intense localized light. With the exception of the attempts at direct suturing, which have not been practicable, all of the methods rely on tissue injury, inflammatory repair, and the production of a chorioretinal scar.

The most popular of these approaches have been the electrical ones, which consist in principle of the use of direct current ("electrolysis") or high frequency alternating current ("diathermy"). The former is in a sense chemical action achieving most of its effect from the irritating reaction of the ions liberated at the cathodic pole. It has been applied with the cathode penetrating the sclera in the form of a thin needle and the anode elsewhere on the body, with both poles penetrating the sclera as fine needles, or transvitreally. Diathermy, as the term implies, produces its effect by heating through the tissues. Whether

the effect is purely one of localized heat production or whether there are also other electrical effects remains to be determined. Attempts are being made, with the aid of the Department of Electrical Engineering at Cornell University, to re-explore some of the basic concepts of current effect on tissue in the various forms now available through modern electronics. The possibilities are most intriguing, but the task appears Herculean when the many problems connected with this aspect of the second objective in retinal detachment surgery are considered.

The third objective, reapposition of retina and choroid, often presents problems. If on bed rest the retina settles back into place, there is little difficulty. It suffices to seal the holes. If excessive damage is not caused by the electrical process, if new holes are not created, and if reasonable postoperative cooperation is obtained, a cure is to be expected. But when the retina does not settle back preoperatively, a complicated problem exists. Something must be done to force reapposition, since without it cure is unlikely. The approaches to this problem fall into two general classes: attempts to force the retina back against choroid and sclera, or attempts to bring choroid and sclera inward to meet the retina. The first class includes various methods of diminishing subretinal fluid or increasing preretinal bulk, or a combination of the two. The second class includes various types of scleral shortening or scleral infolding with or without the insertion of foreign material into or under the sclera or choroid. Removal of subretinal fluid has been tried by many different forms of suction or drainage. Increase in preretinal pressure and volume has been achieved by injection into the vitreous cavity of air, saline, cerebrospinal fluid, and many physiologic solutions. More recently, vitreous transplantation has even been advocated. Various methods of making the outside of the eye come in to reach the retina when the retina will not go back into place have been devised, but there is still room for improvement and simplification. Although it is not the easiest of surgical techniques, Schepens' scleral buckle with plastic tube implant, which yields an axial gain of 0.5 mm. per resected mm., appears to be the most reliable operation now available in difficult cases.

Finally, the many problems connected with vitreous and retinal changes and the part they play in retinal detachment, though they may be the most important, are still the least understood. New means of attacking these problems, however, are now at hand in the form of posterior split-lamp microscopy, electron microscopy, advanced protein chemistry, and radioactive isotopes.

Comment: This short article is a most comprehensive review of the principles underlying the surgery of retinal detachments. The two basic principles of finding the breaks and closing them with chorioretinal adhesions remain the same whatever type of surgery is performed.

Failures in detachment surgery are due to many factors. One of the most important is failure to recognize all of the retinal breaks. The axiom that most detachments are cured with an ophthalmoscope is trite, although there is no question that the prognosis in retinal detachment surgery has improved now that one can see heretofore unrecognized holes with indirect ophthalmoscopy and scleral depression.

With the popularization of the scleral resection and buckling procedures and the use of vitreous implants, many detachments, previously considered hopeless, are being operated. The advantages of performing a scleral resection as a primary procedure are well known. Unfortunately, there are undoubtedly some ophthalmologists who use this as a short cut and get into unnecessary complications. The indications for performing a scleral resection operation have been well described elsewhere. They are not sharply defined and those who do a fair amount of detachment surgery probably do more scleral resection procedures than straight diathermy operations. This is due to several factors: they usually see more complicated cases and they are aware of the hazards of the procedure and can modify the technique as the occasion demands.

Although it has been known for many years that the vitreous plays an important role in detachments of the retina, it has been only within the past few years that we are recognizing certain types of retinal detachments that are due to vitreous contracture. These are cured only by scleral resection, scleral buckling, or vitreous implantation. It is important to recognize these cases and also to be aware that vitreous contracture may follow a so-called "simple" diathermy operation.

There are many unsolved problems in the surgery of retinal detachments. To effect a cure, one must be prepared to spend a considerable time in the preoperative examination of the patient, as well as at the time of surgery. It is not enough to ask the resident to find the break or operate where you think the break is. There is no procedure in ophthalmic surgery that requires more of the ophthalmologist's time. If he cannot afford the time, he should not be performing the surgery.

P. Robb McDonald

AMAUROSIS FUGAX: A SPECIFIC TYPE OF TRANSIENT LOSS OF VISION

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Illinois M. J., 1957, *111:* 21–24

The term amaurosis fugax, defined by Fisher as "periodic blindness in which the principal derangement is an interruption of the retinal blood flow, usually of one eye only," is sometimes used interchangeably with the expression "transient loss of vision." More often however, it is restricted to "a more limited group of cases in which the reduction of blood supply to the retina results primarily from a local disturbance in the retinal arteries or arterioles and not from a lowering of cerebral or general blood pressure." Persons with typical amaurosis fugax have recurrent episodes of usually unilateral blindness, either total or involving a certain sector of the visual field, in which loss of vision is instantaneous, persists for only a few seconds or minutes, and ends almost as rapidly as it begins. The episodes recur with varying frequency, sometimes several times a day, sometimes at intervals of a month or more. Occasionally episodes occur in each eye,

but seldom in both eyes simultaneously. In some instances, after several recurrences, the attacks cease spontaneously. In others, after a varying number of identical attacks, an episode occurs in which blindness persists beyond the usual time and recovery, if any, is incomplete. Ophthalmoscopic examination at this time will reveal ischemic infarction of the retina and ischemic neuroretinopathy.

Presumably, the transient interruption of the retinal blood flow in these cases results from arterial or arteriolar spasm or else from a sudden but temporary decrease in the local arterial pressure in the optic nerve and retina. Early recognition of the cause of the spasm or transient decrease in blood pressure may make it possible to institute appropriate treatment that will reduce the likelihood of permanent blindness.

The stated duration of the periodic episodes of blindness is a distinguishing feature between true amaurosis fugax and superficially similar complaints not based on demonstrable organic disease. Recent studies made by means of electroretinograms controlled by electroencephalograms have shown that the retina of a rabbit can regain full function after 15 min. of ischemia and can regain partial function after from 30–75 min. of ischemia; but that after 105 min. of ischemia no evidence of function can be elicited. Complaints of transient unilateral total or sector blindness with complete recovery in which blindness is said to persist for more than 15, or at most 30, minutes can therefore be justifiably regarded with suspicion.

Ophthalmoscopic examination of the affected eye during an attack of transient loss of vision of the fleeting type is seldom possible because of the short duration of the episodes. Consequently, the diagnosis of amaurosis fugax must be made primarily on the basis of the patient's description of the episodes, and determination of the cause of the syndrome must depend ultimately on the findings of the consulting internist. However, careful study of the ocular fundus between attacks may reveal clues to the origin and nature of the attacks. An atherosclerotic plaque may be visible in a retinal arteriole or the residual of a small nonoccluding embolus; the latter, in the absence of evidence of an active cardiac valvular lesion, may suggest the presence of atherosclerosis either in the central artery of the retina or in the internal or common carotid artery on the side of the involved eye. If the fundi are normal and the patient does not have a history of migraine or Raynaud's disease or a Raynaud-like syndrome, search should be made for possible signs and symptoms of a localized lesion in the common or internal carotid artery and for evidences of temporal arteritis. If either diagnosis can be established, institution of proper therapy (anticoagulants in the first case and cortisone in the second) may prevent permanent loss of vision and, possibly, involvement of other parts of the nervous system. In certain cases, however, in spite of careful study of the patients, it will be found that the cause of amaurosis fugax cannot be discovered.

Comment: The history of repeated fleeting attacks of blurred or "blacked out" vision should never be taken lightly even if the fundi are normal when the patient presents himself for examination. It has been shown that an irritation of the inner surface of an artery or vein by a thrombus or by an endarteritic or endophlebitic process may

cause a widespread reflex spasm of the arterial tree distal to the region of the organic vascular lesion. Wagner believes that such spasms may be a factor in the production of amaurosis fugax preceding the permanent loss of vision in many cases of temporal arteritis.

In intermittent insufficiency of the internal carotid system either reflex spasms from a dislodged thrombotic fragment (Millikan, Siekert, and Shick: Proc. Staff Meet., Mayo Clinic, 1955, *30:* 578) or an unsustained decrease in the local arterial pressure in the optic nerve and retina may produce fleeting visual disturbances. Dynamometric examination occasionally shows a markedly lowered diastolic pressure in the central retinal artery on the side of the carotid insufficiency, sometimes to even less than half of that on the opposite side. It is possible that also in intermittent insufficiency such drops in central artery pressure may occur, causing visual obscurations.

BERTHA A. KLIEN

DETERMINATION OF RETINAL ARTERY PRESSURES IN DIAGNOSIS OF CAROTID ARTERY OCCLUSION

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Neurology, 1957, *7:* 97–104

Although determinations of retinal artery pressure by ophthalmodynamometry were first made 50 years ago, the use of this technique in neurologic and ophthalmologic practice has been limited. The disturbances in vision associated with spontaneous thrombosis of the internal carotid artery have aroused new interest in the circulation of the retinal vessels, and measurement of retinal artery pressures has been suggested as a means of determining the patency of the carotid circulation. Further study, however, was needed to establish the diagnostic value of this procedure, because determinations of retinal artery pressures had previously been made in only a small number of patients with proved impairment of the carotid circulation. Ophthalmodynamometric measurements of retinal artery pressures were therefore obtained in control subjects and in various groups of individuals with impairment of the carotid circulation.

The instrument used in this study was the Bailliart ophthalmodynamometer, which consists of a spring-loaded plunger, the movements of which are transmitted to a dial indicating pressures from 10 to 150 gm. of water. The metal tip of the plunger is applied to the lateral surface of the sclera and the retinal vessels are observed by direct ophthalmoscopy. The first appearance of pulsations of a large branch of the central retinal artery represents diastolic pressure. The subsequent disappearance of pulsation with increased pressure on the sclera in-

dicates systolic pressure. Mydriatics are generally used, but local anesthesia is not necessary. The examination is carried out with the patient in a supine position. At least two and usually three measurements are made in each eye, depending on the constancy of the readings. An effort is made to obtain the readings in rapid succession to avoid alterations in intraocular pressure which might result from prolonged compression of the globe. The average of these readings is used in comparing the retinal artery pressures in the two eyes.

Analysis of the results obtained showed that patients with arteriosclerotic narrowing or occlusion of the internal carotid artery had significantly lower retinal artery pressures in the ipsilateral eye. Surgical ligation or gradual occlusion of the carotid artery also produced measurable alterations in the ipsilateral retinal artery pressures.

Although the height of the retinal artery pressure depends largely on the systemic blood pressure, there was only one subject in whom the systemic pressure was too great to permit ophthalmodynamometric readings to be obtained. The suggestion has been made that the brachial artery pressures should be determined at the time of examination of the retinal artery pressures. Since a difference in brachial artery pressures does not detract from the significance of a difference in retinal artery pressures, such determinations seem unnecessary as a routine procedure. They might, however, disclose the presence of an aortic arch syndrome or an innominate artery thrombosis in which the circulation in both the brachial artery and the carotid artery was impaired. Bilateral occlusion of the carotid arteries is not uncommon in the aortic arch syndrome, and when it exists, the retinal artery pressures of both eyes may be too low for satisfactory comparison. The method used in this study is a comparison of the pressures in one eye with those in the other, and its validity is based on the assumption that the circulation in one carotid artery is comparatively intact.

The degree of accuracy of ophthalmodynamometry may be reduced by minor errors in technique, some of which deserve to be emphasized. To allay apprehension, the procedure should be explained to the patient and application of the plunger to the sclera should be demonstrated before the actual determination. Care should be taken to avoid interpreting venous pulsations as representing diastolic pressure. Erroneous determinations of the systolic and diastolic end points are often made in patients with bradycardia or cardiac arrhythmia. The degree of reduction in retinal artery pressure necessary to establish a diagnosis of carotid artery occlusion cannot be stated in absolute values. In a cooperative subject, however, in whom the exact time of appearance and disappearance of arterial pulsations can be accurately noted, a reduction of 25 or 30 per cent in both systolic and diastolic pressures is diagnostic of impaired carotid circulation. A similar reduction in either the diastolic or the systolic pressure should be regarded as confirmatory evidence in patients with the clinical picture of carotid artery disease. Some workers have recommended that only the diastolic pressure be used as the diagnostic criterion, since the appearance of arterial pulsations can be determined more accurately than their disappearance. In this study, both systolic and diastolic pressures were of value, because some patients with impair-

ment of the carotid circulation showed a decrease in systolic retinal artery pressure only. This was particularly true in patients with incomplete occlusion or with slight narrowing of the vessel.

Retinal artery pressures have been found to correlate well with direct carotid pressure readings at the time of surgical ligation, and ophthalmodynamometry has been suggested as a means of estimating the degree of collateral circulation after ligation of the carotid artery. It does not seem likely, however, that this procedure can be depended upon to show the extent of the decrease in cerebral circulation after carotid ligation or to provide a basis upon which to predict the safety of ligation in certain cases. The possibility that long-term ophthalmodynamometric observations of patients with carotid ligation may provide useful information as to the appearance and degree of collateral circulation is now being studied.

The only complication encountered in this study was a mild subconjunctival hemorrhage in one person following application of the instrument. While it is possible that retinal detachment and thromboses of the retinal vessels may follow prolonged or too vigorous pressure on the sclera, such complications must be extremely rare and none are known to have been reported. Despite these potential hazards, the value of the procedure is great enough to warrant its use as a diagnostic method.

Comment: In order to establish a diagnosis of carotid artery disease from the results of dynamometry one has to rule out lesions of the ipsilateral central retinal artery, which also might produce a lowering of the diastolic and systolic pressures.

Dynamometry should be accompanied by a detailed study of both fundi. Any evidence of possible central retinal artery disease such as unilateral attenuation of the retinal vascular trees, or retraction of the first bifurcation of the central artery backward into the optic papilla would render the dynamometric findings less valuable for diagnostic purposes.

The recent revival of dynamometry may, however, result in valuable information concerning the speed of development and the effectiveness of collateral circulation in patients with carotid ligation, especially when carried out over long periods on the same patient.

BERTHA KLIEN

THE SLUDGING OF BLOOD IN THE RETINAL VEINS

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Lancet, 1957, *1:* 65–66

Visible sludging or clumping of the red blood cells in the retinal veins is a non-specific sign which may occur when the blood flow has been slowed by pressing on the eye.

To elicit the sign the vessels at the optic disc are viewed through an ophthalmoscope and pressure is exerted with the thumb of the free hand on the lateral aspect of the upper eye lid. The pressure required is only enough to induce partial diastolic collapse in the retinal arteries. When the sign is positive the column of blood in the veins becomes at first granular and then forms into larger discrete particles which move slowly toward the disc. The time required for these to appear is five to eight seconds and there is no point in prolonging the pressure if no response is elicited.

Sludging was observed in 90 patients on one or more occasions (Table 1). Of these 79 had definite organic disease and in 11 no disease was found.

Sludging was not seen in 31 healthy persons and 150 out-patients with disorders as shown in Table 2.

The phenomenon occasionally occurs in pregnancy and during menstruation when no other disorder is found.

Table 1

Disease	No. of Cases	Disease	No. of Cases
Active tuberculosis	17	Systemic lupus	3
Carcinoma	10	Reticulosis	3
Cirrhosis	6	Leukemia	2
Bronchiectasis	6	Myocardial infarction	2
Myelomatosis	5	Ulcerative colitis	2
Pyrexia of undetermined origin	5	Miscellaneous	10
Pneumonia	4		
Rheumatoid arthritis	4	Total	79

Table 2

Disorder	No. of Cases	Disorder	No. of Cases
Functional disorders	33	Angina of effort	6
Peptic ulcer	17	Infection of renal tract	6
Neoplasm	9	Hiatus hernia	5
Chronic bronchitis	8	Miscellaneous	51
Spondylosis	8		
Hypertension	7	Total	150

Elevation of the erythrocyte sedimentation rate and serum globulin was found in some patients with sludging but the correlation was not close. A better index existed between the clinical condition and the sludging as the test seems to be a fairly reliable index of organic disease.

Comment: The difference between spontaneous sludging of the blood in the retinal veins and sludging produced by pressure upon the eyeball, such as the author discusses, may be only a matter of degree.

Both types of sludging are produced by an increased coagulation of erythrocytes in slow circulation. Spontaneous sludging may be the consequence of greater friction among an increased number of cellular constituents of the blood as in the leukemias and lymphosarcoma, or of an increased serum viscosity as in the macroglobulinemias (multiple myeloma, Waldenstrom's type, etc.), or the slowing may be caused by widespread arterial spasm in thromboangiitis obliterans. A classical example of the latter would be the pulseless disease.

Your commentator has observed sludging of the venous column of several days duration in a patient with diabetes and generalized arteriosclerosis after a severe internal hemorrhage in the course of anticoagulant therapy. The sludging in this case was unilateral and preceded by marked transient narrowing of the retinal arterioles and temporary loss of vision in this eye.

Sludging elicited by pressure upon the eyeball may have diagnostic implications similar to the spontaneous type, but pointing to milder, "subclinical" degrees of the same conditions.

BERTHA A. KLIEN

THE FUNDUS OCULI AND THE DETERMINATION OF DEATH

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Am. J. Path., 1956, *32:* 1253–1269

Pathologists and clinicians alike are made aware all too frequently of the need for a simple and readily available method for determining whether death has occurred. While a condition of "suspended animation" does not exist in the literal sense, respiratory and circulatory activity may be so reduced in both rate and intensity as to escape detection by the usual procedures. The possibility of resuscitation time may not permit the use of an electocardiograph or similar apparatus.

Three cardinal signs occurring more or less concomitantly but at different velocities and with different degrees of intensity comprise the so-called ophthalmoscopic signs of death. These are signs of cessation of blood flow to the bulb and, inferentially, of cessation of cardiac output.

Disappearance of the retinal artery and its central branches. As the circulation

slows down with gradual failure, the arterial blood columns become "granular" due to the visibility of clumped, rapidly moving erythrocytes. They may eventually form "beads" or become "striated" at the instant of heart standstill; at the same time the caliber becomes markedly reduced. As a rule the arterial pattern disappears rapidly, perhaps within the following minute or less, although it is reported to have persisted for much longer periods with the initial onset of peripheral arteriolar haziness. Arterial blood, when seen, remains brighter than that in the veins.

Color changes in the retinal and choroidal layers. At the instant when circulation stops, the choroid becomes pale yellow-orange; and the optic disc immediately becomes white and sharply outlined. Grayish retinal turbidity begins to appear rapidly, at first in the posterior pole of the globe around the disc, gradually progressing to the periphery where some red tinting may be perceptible even hours after death. The macula appears as a red spot on a field of delicate gray-yellow, then gray-white and deep gray after several hours.

Retinal venous changes. As in the arteries circulatory deceleration results in "granularity" of the blood columns of the retinal veins. Almost without exception these columns break into segments ("beads," "striations") within a few seconds after circulatory stagnation. Such formations are seen chiefly in the larger veins at or near the disc, although the site is variable. The segments and clear spaces between continue to move smoothly for 10–20 min. after their evaluation and finally become static. They remain visible for several hr. Hours later the final picture is one of magenta colored venous segments on a uniformly gray retina which shows no trace of an artery.

These signs, particularly "granularity" and segmentation of the veins signify only one thing: absence of cardiac output. Segmentation with movement is of the utmost importance in resuscitable cases. No known clinical or laboratory aid other than the ophthalmoscope can indicate so quickly whether circulation has stopped recently enough to allow for resuscitation without residual central nervous system disintegration.

Comment: The determination of death by means of ophthalmoscopy is a subject which has not been discussed in recent years. However, with the widespread use of cardiac massage for resuscitation and the increasing popularity of general anesthesia in ophthalmology it is of obvious importance. Each well equipped ophthalmic operating room should have an ophthalmoscope to examine the fundi of children being operated for strabismus. (It is surprising how frequently this step is neglected although complete examination of the fundi is frequently not possible in these patients until they are asleep.) With the ophthalmoscope quickly available the diagnosis of cardiac arrest may be made many seconds before other signs become obvious. The author of this interesting paper believes that resuscitation is possible as long as the segments of blood are moving in the veins—possibly 10–20 min. after the heart has stopped. This is a much more generous time estimate than usual—many feel that circulation by cardiac massage must be established before three minutes have elapsed or that irreversible brain damage occurs. Beck (J. A. M. A. 1957, *163:* 875) points out that the catastrophe of cardiac arrest may complicate any type of operation and that "every surgeon and every anesthetist can expect to encounter it (cardiac arrest) in the operating room some time in his professional career."

When it occurs the first step required is the insertion of a tube into the trachea and the inflation and deflation of the lungs by compressing a rubber breathing bag filled with oxygen. Next the chest must be boldly opened and the pericardium incised and the heart pumped by hand. All of us hope that it will never be our lot to carry out these procedures but one must be prepared beforehand since there will be no time for study at the time such an emergency occurs.

F. W. N.

Hereditary Disease

OCULAR ABNORMALITIES IN PROGERIA

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Acta ophth., 1956, *34:* 347–354

Progeria, which becomes manifest between the ages of 2 months and about 3 years in children with no abnormal genetic dispositions, consists of a combination of infantilism, premature senility, and well-proportioned dwarfism. Scanty hair growth, few or lacking eyebrows and eyelashes, and thin atrophic skin with distinct venous pattern bear witness to the premature senility. The patients are often likened to plucked birds, in reference to their baldness and peaky facial features; the face is compressed from side to side and dominated by a high forehead and arcuate nose, sometimes being flanked by low-placed projecting ears. The lower part of the face, more particularly the mouth and the lower jaw, is senile atrophic and diminished, creating a hydrocephalic appearance in spite of the normal circumference of the skull. The children, who are in most cases said to be intellectually normal, are generally somewhat emaciated, with a large abdomen and narrow shoulders.

Duke-Elder and Walsh seem to be agreed that progeria is generally not associated with any characteristic ocular disorders; nevertheless, in a condidition with such extensive changes, it is only natural that the ocular findings should at times be pathologic. At the Ophthalmologic University Clinic of the Rigshospitalet and at the Ophthalmologic Clinic of the Royal Institute for the Blind, it has been possible during the last 20 or 25 years to watch three patients with progeria suffering from various ocular disturbances. Two of these patients have previously been described in detail from a pediatric point of view; consequently, the discussion in this paper is confined to the ophthalmologic conditions.

When first examined at the age of about 12 months, patient no. 1 was found

to have bilateral microphthalmos, with arcuate cornea and microcornea. The pupils in both eyes were also small, with persistent star-shaped membrane and congenital nonhereditary cataract. The second patient was examined for the first time at the age of 5 years. She did not suffer from congenital cataract, but in other respects the ocular findings were in close harmony with those of patient no. 1. Microphthalmos associated with microcornea and arcuate cornea was found; the eyebrows and lashes were scanty; the eyes protruded; and nystagmus and convergent strabismus were present. The third patient, who was 3½ years old on admission, was the least interesting from the ophthalmological point of view, because, apart from scanty eyebrows and eyelashes and a variable convergent strabismus, the eye examination of this child revealed perfectly normal conditions.

The first two patients seem to be the only ones in whom the existence of microphthalmos, microcornea, and arcuate cornea has been reported. All three patients had scanty or lacking eyebrows and lashes, as well as convergent strabismus, which was complicated in the first two with irregular nystagmus and slightly protruding eyes. Several investigators have emphasized the presence of prominent ocular bulbs, which is probably due to a lack of space in the orbit and atrophy of the subcutaneous tissue. The first two patients have also had late-appearing ocular disturbances, beginning at the age of 15 and 20 years, so that both are incapacitated because of defective vision (visual acuity in the first is light sense plus projection in the right eye and 2/24 in the left eye; in the second, it is 1/18 and 1/24).

Patient no. 1 has presented a pale optic papilla and small pigmentations in the retina during the last 3 or 4 years. In patient no. 2, a membranous conversion of the lenses with formation of whitish, wartlike excrescences at the edge of the pupils has been observed during the last 10 years. These changes bear no resemblance to senile exfoliation and must presumably be the result of a defective genetic disposition with regard to the lens. For the last 6 months, this patient has also been suffering from glaucoma of the right eye.

The ocular abnormalities found in these patients may parallel the findings of familial appearance of a mild microcornea, corectopia, and congenital glaucoma and opaque cornea in a group of patients described by Franceschetti and coworkers as "a new biotype of progeria." It may also be that ocular disturbances in progeria occur more frequently than has hitherto been believed.

Comment: The progeria of Gilford is a particular form of dwarfism in which the affected individual presents an unusual combination of signs and symptoms of both infantilism and premature senility. In addition to the nanism there coexists infantile proportions of the skeleton, hypognathus, atrophic skin changes, and absence of secondary sex characteristics. In general the gonadal development, the musculature and intelligence are within normal limits. Considerable variation in expressivity, as is true of most syndromes, is reported.

Gregersen includes ectodermal dysplasia and Werner's syndrome in his differential diagnosis and in his discussion also calls attention to the close similarity of his cases to those reported by Hallerman, Nizetic and Strieff.

The Hallerman-Strieff syndrome is chiefly characterized by a congenital nasal deformity which simulates a parrot's beak (underdevelopment of the cartilaginous alae of the nose), hypognathus, microphthalmia, and congenital cataract. In addition, in a case of the commentator's, localized hypotrichosis, nystagmus, "secondary" cataractous membranes, high pitched "cracked" voice and external ear aberrations were observed. Ullrich and Fremerey-Dohna also noted localized hypotrichosis in their case with associated sutural skull defects.

Because of the frequency of congenital and ocular aberrations present in Gregersen's cases I should like to suggest, on very tenuous grounds, that they are examples of the Hallerman-Strieff syndrome rather than progeria.

The frequency of bilateral spontaneous absorption of the cataractous lens in the Hallerman-Strieff syndrome is extremely noteworthy.

HAROLD F. FALLS

EPIBULBAR DERMOIDS–PREAURICULAR APPENDICES COMBINED WITH UNILATERAL MALFORMATION OF THE FACE

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Acta ophth., 1956, *34:* 412–420

Congenital malformations of the facial skeleton may appear in various groups and combinations, some of which are found in more or less well defined syndromes, while others are incomplete or atypical. The characteristic defects in Franceschetti's mandibulofacial dysostosis (Treacher Collins syndrome), for example, have been listed as follows: (1) a downward lateral (antimongoloid) slope of the palpebral fissures, with a coloboma in the lateral portion of the lower lid, more rarely in the upper lid; (2) hypoplasia of the facial bones, especially the malar bones and the mandible; (3) malformation of the external ear, and occasionally also of the middle and inner ears; (4) macrostomia, high palate, abnormal position and malocclusion of the teeth; (5) blind fistulae between the corners of the mouth and the ears; and (6) atypical growth of the hair, which extends downward like a tongue toward the cheeks. Other skeletal deformities and facial clefts may also be found in some patients.

In 1952, Goldenhar studied the simultaneous occurrence of malformations in the ocular and aural regions, with special reference to a syndrome of epibulbar dermoids–preauricular appendices and congenital aural fistula and its relation to mandibulofacial dysostosis. He described three cases of the fully developed syndrome and 30 cases of epibulbar dermoids–preauricular appendices, 16 of which were combined with other malformations, chiefly localized to the face. A survey of the literature has revealed eight additional cases in which epibulbar

dermoids (conjunctival lipodermoids, limbal dermoids) and auricular malformations were combined with unilateral hypoplasia of the face. In only two of these cases were the epibulbar dermoids described as bilateral symmetrical lipodermoids; consequently, it seems worth while to report the discovery of lesions meeting this description in two patients seen by the author.

The first patient, a generally healthy 20-year-old girl, with a left-sided facial hypoplasia, had during the last few years noticed some nodes in both temporal canthi. On examination, the nodes, which had slowly increased in size, were found to be flattened, pale yellowish-red, soft, movable swellings that proved to be lipodermoids. In addition to the various defects caused by the left-sided hypoplasia, two small preauricular appendices were present in front of the left tragus. Radiography of the skull showed unilateral hypoplasia of the left ramus and collum of the mandible.

The second patient, a 17-year-old girl with a left-sided facial malformation, who had had no serious illnesses during childhood, sought advice for cosmetic reasons. Examination of the eyes showed bilateral epibulbar dermoids, partly in the form of symmetrical lanuginous lipodermoids in the temporal canthi and partly in the form of limbal dermoids situated at 3 o'clock, the one on the right being larger than that on the left. The external ears were rather low-seated and the connection between the tragus and the lobule was deformed; the external meatus on the left was short and deficiently developed. Preauricular appendices were found in front of both ears. The one on the right, which measured 3 by 5 mm., was rounded and soft, connected with the lower part of the tragus by a short stalk. The one on the left was about the same size; it was also soft but was flatter and in front of it there was a blind preauricular fistula. Radiographic study showed unilateral hypoplasia of the left ramus of the mandible and its collum; no temporomandibular articulation could be found.

Classification of these cases within the principal syndromes of facial dysprosopia would be difficult, because as often happens they contained features that are characteristic of several; thus the oculoauricular malformations must be grouped with the syndrome established by Goldenhar. The unilateral asymmetry suggests the unilateral form of Franceschetti's syndrome, but a number of the criteria were lacking. Consequently, these cases must be classed as belonging in the syndrome of epibulbar dermoids–preauricular appendices, combined with features resembling those of the unilateral form of Franceschetti's syndrome, so that they represent a transition type between the two syndromes.

The occurrence of the simultaneous oculoauricular changes can easily be understood when it is borne in mind that from the fourth to the sixth embryonic week the structures involved are found in close relation to each other on the lateral side of the embryo's head and neck (the processus nasalis medialis and lateralis are uppermost; then follow the optic vesicle, and, lowest, the first and second branchial arches with the intervening first branchial furrow). It therefore seems reasonable to assume that the underlying embryonic lesion in these cases is the same, and that the difference in phenotype is a question of where the lesion has exerted its maximum effect.

Comment: Axel Mahneke has aptly discussed the congenital malformations of the facial and skull skeleton and has contributed two additional cases to the literature. The author admits that his two cases defy classification, stating "a classification of the cases reported here within the dysprosopias would meet with difficulties, as the complex of symptoms described cannot be referred to any one of the more well-defined syndromes since, as is often the case, it presents features which are characteristic of several of these." He assumed "that the underlying 'embryonic lesion' in these cases is the same and that the difference in phenotype is a question of where the 'lesion' has exerted its maximal effect."

Since similar statements are being more frequently encountered in the literature it is perhaps profitable, herewith, to discuss causation of variation of expression of a syndrome as well as so-called intermediate forms. Most physicians recognize the fact that the same bacterial causative agent may affect any or several of a variety of effects and in addition a marked variability in severity of affection. It is, however, not frequently recognized that analogous phenomena are manifested by the action of genetic factors. Variability in the type of manifest effect of a particular gene or gene complex (phenotype) in specific individuals has been termed *expressivity*, the term being used in reference to the *degree* of severity of expression in a particular individual. Study in the laboratory of mammals as well as other animals has disclosed that the expression of many genes can be influenced by a variety of factors both environmental and genetic (modifiers). It is recognized that there is a dependence of all aspects of gene expression on conditions of the prenatal or postnatal environment (maternal age, temperature, nutrition, susceptibility to infection, hormones, sex of fetus, and so forth). Aberrations of development which simulate gene determined entities but which are produced by the action of abnormal or artificial environmental agents upon any of a wide variety of genotypes are termed *phenocopies*. Such represent the effects of environmental variables and agents (temperature, irradiation, infection, and so forth) on the expression of genetic factors. The resultant, a *phenocopy*, depends upon the *stage of development* of the fetus (period of organogenesis)—nature, intensity and duration of the effect of the environmental noxious agent in addition to the genetic constitution of the fetus. The expression of almost any gene or gene complex is also influenced, furthermore, by the nature of the individual's gene milieux [other genes at different loci (genotype)]. A modifying gene or polygenic modifiers may thus alter the phenotypic expression of a single gene or gene complex.

There are, thus, many ways in which a given genetic determined trait may be modified in its expressivity—genetic modifiers and environmental agents. Any syndrome dependent upon a single gene determination may vary conspicuously in expressivity from individual to individual dependent upon both environmental and genetic influences.

Another possibility, which must be considered, is that different *main* genes may produce a similar phenotype but not through similar enzymatic actions and thus subtle variation in phenotype results. Since each individual is a law unto himself as to genotype, time and speed of organogenesis, rate of development and so forth, similar genes should be anticipated to exert their actions in minutely different substrata and thus minor end-product variations are always to be expected. Lastly, mutation of a normal gene may vary slightly from mutation to mutation.

Variability in expressivity, even intermediate stages between syndromes, result from variations in environment and genetic make-up of each affected individual which influence and modify the action of any single gene.

HAROLD F. FALLS

SYSTEMIC DISEASE

MANAGEMENT OF EXOPHTHALMOS AND RELATED OCULAR CHANGES IN GRAVES' DISEASE

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Metabolism, 1957, *6:* 36–48

Modern methods of controlling the hyperthyroidism in Graves' disease are so safe and quick that the accompanying exophthalmos and other ocular manifestations of the disease are now one of its most troublesome features. This is because a preponderance of the patients are women and to women of any age the disfigurement of conspicuous eye signs is a source of acute mental suffering. Furthermore, in the severe ophthalmic forms infectious complications occasionally lead to total blindness.

The management of exophthalmos must be based on sound methods of observation. Actual measurement of the ocular changes should be part of the routine for all toxic goiter patients and the necessary armamentarium should be found in every well equipped clinic. Purely descriptive notes will not provide a reliable guide during management. There are too many pitfalls. For example, sympathetic stimulation in man does not cause exophthalmos though retraction of the lids occurs, exposing an abnormal extent of the eyeball's surface. Similarly in states of stress or anxiety the eye may look as if it were starting out of its socket, even though its position is unchanged. Factors such as these may account for the claims still heard, but not confirmed by measurements, that exophthalmos may develop abruptly, even overnight, or that it may fluctuate rapidly.

Whatever the methods of measurement that are used, the prime consideration is that serial measurements adequately covering the orbital condition must be made. The patient attends monthly, or oftener if complications threaten. At each visit, she is asked to close the lids lightly and the examiner ascertains whether the lid margins meet easily and remain apposed. Failure of the lids to meet is a sign of the first importance. It may be due simply to spastic lid retraction, in which case the conjunctiva usually remains almost clear and there is little threat of exposure or infection. Or, more seriously, it may be the result of the severity of the exophthalmos, or of interposition of prolapsed conjunctiva, or of a combination of all these factors. In any case, if the lids fail to appose easily, the eye probably remains open during sleep and some degree of conjunctivitis is usually apparent. Exposure effects, including desiccation and keratitis, may follow. These always imply a threat to vision and must be vigorously controlled.

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The tension on the globe and lids, as indicated by their mobility on the subjacent orbital tissues, should be especially checked. This is done by light digital pressure on the eyeball through the closed lids. Orbitonometry may be used to obtain quantitative data. Fortunately, in most patients with even high degrees of exophthalmos, the lids remain lax and the eyeball freely mobile, but in some subjects the palpebral fissure is naturally small and the tone of the lids and their ligaments is firm. With marked orbital tissue enlargement, the lids may then become exceedingly tight and stretched with corresponding counterpressure on the whole of the orbital contents. The orbit is overcrowded to the point of being packed solid. Edema, infection, and prolapse of the conjunctiva then commonly occur and there is a real danger of loss of sight in the eye as a result of rapidly progressive infectious complications, corneal ulceration, hypopyon, and panophthalmitis.

When characteristic eye signs occur with goiter and hyperthyroidism, the diagnosis of Graves' ophthalmopathy may be accepted. But when hyperthyroidism is lacking, especially if the exophthalmos is unilateral, other causes should be considered. Without discussing the differential diagnosis in detail, it may be pointed out that the conditions most commonly confused with the ocular manifestations of Graves' disease are orbital tumors or similar space-occupying lesions in or encroaching on the orbital cavity, caroticocavernous fistula, arterial aneurysm, and myasthenia gravis. The features most characteristic of Graves' ophthalmopathy are spastic lid retraction, the pattern of the ophthalmoplegia, and the essentially bilateral distribution of the eye changes. Radiological examination of the orbits and cerebral arteriography fail to reveal any abnormality in patients with Graves' disease. Incidentally, whenever the question of orbital decompression arises, radiographic study is needed to determine the size and location of the frontal, ethmoid, and maxillary sinuses, because the surgeon may elect to avoid entering them in the course of the operation.

Unfortunately, no rational attack can yet be made on the basic hormonal upset responsible for the ocular changes, nor is any drug, hormone preparation, or other therapy used empirically of proven value. Ocular disturbances often occur in patients undergoing stress, and then general measures aimed at social adjustment and relaxation of tension are obviously indicated. If the eye changes are managed carefully, the ultimate cosmetic outlook is generally very good. The patient should be constantly reassured on this point.

The author's policy is to treat the thyroid status on its own merits, controlling hyperthyroidism if it exists. If the eye trouble is severe, long-term antithyroid drug therapy is the method preferred, because it eliminates the risk of inducing irreversible hypothyroidism. If the patient is already hypothyroid, as in some cases of post-thyroidectomy "malignant" exophthalmos, thyroid extract is given to restore euthyroidism.

Certain difficulties are encountered in assessing the value of the various forms of empirical therapy and local palliative measures. Thus the behavior of exophthalmos after thyroidectomy in two otherwise untreated patients was entirely different: in one, the level of the exophthalmos declined steadily from the time

of the operation, while in the other control of hyperthyroidism was followed by further steady protrusion of the eyes. Moreover, if treatment is to be long continued, allowance must be made for the natural tendency of the ocular changes to become static or to regress. Another difficulty lies in the fact that after a dynamic phase, the ocular changes may persist in a static phase for years, so that a form of treatment that would be effective in one phase might be ineffective in the other.

Since treatment with drugs or hormones is still experimental, it is necessary to fall back on local palliative measures. At certain stages, close collaboration with an ophthalmologist or neurosurgeon is needed, but the treatment must be directed by the thyroidologist, and he should therefore understand all the moves. The guiding principle is to minimize the effect of the pathologic changes during their dynamic phase and subsequently to correct residual disabilities such as persistent squint. Fortunately, the eye trouble remains mild or moderate in all but about 5 per cent of the patients. It is precisely in the mild or moderate cases, however, that the simplest and most beneficial treatment is neglected, namely, the use of cosmetic spectacles. These have appropriately tinted lenses incorporating any refractive correction that may be necessary and are attractively shaped. Such tinted spectacles not only conceal the patient's disfigurement but may even add to her natural feminine attractiveness. They should be advised routinely at an early stage to prevent the patient from ever feeling self-conscious or embarrassed about her appearance. The tinting should not be such as to cause strong pupillary dilatation in patients threatened with glaucoma and the use of the spectacles at home should not be so continuous as to render the eyes light-sensitive. Moreover, the refractions should always be checked. When cosmetic spectacles are carefully chosen and prescribed according to these principles, the mental relief they provide can scarcely be calculated.

The principal dangers in cases of severe ophthalmopathy are exposure and infection of the conjunctiva and the cornea, and extreme tension on all the orbital contents. These developments should be anticipated and prevented by prompt tarsorrhaphy and wide orbital decompression. If the vision can be preserved, the ultimate prognosis for functional and cosmetic recovery is good. Correction of residual stigmata should be left until the orbital changes have reached a static phase. An ophthalmic surgeon, using comparatively minor procedures, can then do much to restore sensibly normal function and appearance. Residual squints, in particular, should be corrected surgically.

Comment: This paper presents a plea to endocrinologists to follow the exophthalmos of their thyroid patients more closely. It is suggested that this be done in more objective and quantitative fashion by serial measurements.

The medical means of handling progressive thyrotropic exophthalmos, such as the administration of thyroid or cortisone or the injection of hyaluronidase, have in general proved most unsatisfactory. Radiation of the pituitary or of the orbits has also failed to halt the progress of this disease process. In those instances where spontaneous regression does not occur, patients should be followed closely for ocular damage from pressure or exposure. When necessary, surgical decompression may be readily accomplished and

provides dramatic relief. In addition to the intracranial and temporal approaches, which have been emphasized repeatedly, very striking improvement can also be obtained by decompression of the orbit from below into the maxillary sinus. The inferior approach can be done under local anesthesia and without skin incision, and provides excellent cosmetic and functional results.

BERNARD BECKER

OCULAR MANIFESTATIONS OF SARCOIDOSIS

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Cleveland Clin. Quart., 1957, *24:* 10–16

Sarcoidosis is a ubiquitous disease of unknown etiology that affects young adults of both sexes. One of its characteristic features is a lack of direct correlation between the severity of the symptoms and the extent of the disease. The general health of the patient is often good, although he may lose some weight and have periods of fever.

Ocular lesions, found in about 50 per cent of the patients affected by sarcoidosis, may appear in almost any part of the eye, but the most frequent ocular manifestation of the disease is inflammation of the anterior uveal tract. There is no relation between the onset of the ocular inflammation and that of any other manifestation of sarcoidosis. The iritis is usually painless, inflammatory symptoms are slight, and synechia is common. The typical clinical picture is that of a nodular type of iritis. The nodules, which are usually superficial but may lie deep in the stroma, differ in certain respects from true miliary tubercles. Large keratitic precipitates of the mutton-fat type are typical of sarcoidosis. Inflammation may be accompanied by the development of a heavy plastic iritis. If the parotid gland becomes swollen, Heerfordt's disease (uveoparotid fever) develops. Palsies of the cranial nerves, especially of the facial nerve, may also appear.

A study of 11 patients with ocular manifestations of sarcoidosis treated at the Cleveland Clinic during the last 7 years showed that evidences of active anterior uveitis were present in 10, 3 of whom also had uveoparotid fever. Most of the laboratory findings were typical of sarcoidosis. Anergy to tuberculin was demonstrated in 8 of the 9 patients tested; the result in one patient was not recorded. The results of the Kveim test were positive for sarcoidosis in 6 of the 9 patients given this test; in two, the result was negative and in one it was not recorded. In one of the patients in whom the result was negative the sarcoidosis was thought to be in a state of remission; in the other, it was found that a weak, equivocal antigen had been used. Abnormalities, consisting mostly of involvement of the hilar lymph nodes, were present in the chest roentgenograms of 10

of the 11 patients. When a patient with a granulomatous type of iritis demonstrates anergy to tuberculin, sarcoidosis should be suspected and special diagnostic tests, especially the Kveim test, should be performed in addition to the routine diagnostic procedures.

The treatment received by the patients reflected the therapeutic progress made during the period. The patient seen earliest received no medication for her systemic disease. Atropine and merthiolate ointment were recommended for topical treatment of her eyes, but she was examined only once, and the results of treatment are unknown. Two of the other early patients (patients 3 and 4) received calciferol. It is not known what treatment, if any, patient no. 2 received for iritis, and the only known systemic treatment was irradiation to the chest given in another hospital to prevent the development of Hodgkin's disease. In patient no. 3 atropine alone, topically applied to the eyes, produced excellent improvement in the severe iritis from which she suffered. In patient no. 4, it was recommended that the pupils be kept dilated with atropine, but the results are not known. In five patients (5, 6, 7, 8, and 11) most recently seen, iritis was treated by topical application of cortisone and atropine. In each, the iritis subsided, although there was mild recurrence in some cases. Patient 5 obtained a remission of her generalized disease after a course of nitrogen mustard therapy. Patient 6 received cortisone orally and has since had no systemic manifestations of the disease. Patient 7 received a short course of cortisone orally and corticotropin (ACTH) intramuscularly, followed by a longer period of isoniazid therapy administered orally; her condition also improved. The administration of isoniazid to patient 8 was stopped after two months when iritis developed, and treatment with orally administered cortisone and local applications of cortisone and atropine was instituted. This treatment proved effective and the patient became symptom-free. Patient 11 is now receiving only isoniazid systemically, and his skin lesions are disappearing. The 10th patient, who was the only one without manifestations in the uveal tract, was found to have a large mass covering the optic disk in the left eye and old chorioretinitis in the right eye. Although he has been given cortisone, corticotropin, and isoniazid systemically, his condition has not yet shown any improvement. Apparently, the extent of the ocular involvement is so great that there can be little hope for any appreciable restoration of function in the optic nerve.

Although there is no specific remedy for sarcoidosis, patients with ocular manifestations of the disease should always be given systemic therapy. Isoniazid and cortisone appear to be the best medicaments now available, but an increased tendency to bleed has been reported as occurring in some patients receiving isoniazid. The possibility that retinal hemorrhages may occasionally develop as a part of isoniazid intoxication should therefore be kept in mind.

Iritis caused by sarcoidosis is probably best treated by local applications of cortisone and atropine. This treatment was successful in bringing about a remission of the iritis in all five patients in this series to whom it was given.

Comment: This report represents an abstract of a thesis reviewing the literature on sarcoidosis and its ocular manifestations. The widespread systemic and ocular signs and

symptoms of this granulomatous disease process are emphasized. Eleven cases with uveitis and other ocular involvement are summarized and their improvement with steroid therapy demonstrated.

In one patient (no. 10) in the present report, a large mass covered the disc. This recalls the recent publication of two similar cases where compression of the nerve head by large nodules led to visual loss. (Morax, P. V., Ann d'ocul., 1956, *189:* 73.)

The present paper neglects the very interesting ocular signs seen in the hypercalcemia associated with sarcoid in some patients. The appearance of calcium deposits in the cornea and conjunctiva, as described by Walsh and Howard (1947), can be visualized readily by slit lamp examination. Furthermore, these deposits disappear when the blood calcium level is lowered by steroid therapy or dietary means. (Crick, R. P., Trans. Ophthal. Soc. United Kingdom, 1955, *75:* 189.)

Recent studies on sarcoidosis have revealed a much greater incidence of skeletal muscle (Phillips, R. W., and Phillips, A. M., A.M.A. Arch. Int. Med., 1956, *98:* 732.) and conjunctival follicular involvement (Crick, R., Hoyle, C., and Mather, G., Brit. Med. J., 1955, *2:* 1180.) than previously suspected. These biopsy sites should be considered in addition to the conventional skin and lymph nodes in establishing the diagnosis of sarcoid.

BERNARD BECKER

CONTRIBUTION TO KNOWLEDGE OF DIABETIC DISEASES OF THE VESSELS OF THE EYE

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Ophthalmologica, 1957, *133:* 109–118

Twenty-two of 101 patients with diabetes mellitus showed characteristic changes of retinopathy in their eyes. Twenty per cent of the 22 patients also had aneurysms of the conjunctival vessels. The duration of diabetes mellitus as the primary disease was 10 years or more in 14 (64 per cent) of the 22 patients. This ratio can be considered as relatively low, since retinopathy may usually become manifest only after 10 yr. This is particularly true of cases occurring in adolescents. In four of the 22 patients, the retinopathy was observed after a duration of the diabetes mellitus for 5 yr., and in 4 others after a duration of from 5 to 10 yr. In 7 of these 8 patients, the diabetes mellitus began after the age of 50 yr. These findings seem to suggest that the "age of arteriosclerosis," i.e., the age from 50–60 yr., may exert an influence on the occurrence of diabetic angiopathy of the retina. Changes in the vessels do not play the same part in the genesis of retinopathy in juvenile persons as in adult persons in whom arteriosclerosis is of particular importance.

The duration of the primary disease was also significant in the 14 patients who have had diabetes mellitus for more than 10 yr. Retinopathy was observed in 2 with a duration of diabetes mellitus of from 10–15 yr., in 6 with a duration of diabetes of from 16–20 yr., and also in 6 with a duration of more than 20 yr. The 14 patients with retinopathy after more than a 10-year duration of their primary disease (*group a*) were compared with 27 patients without retinopathy under the same conditions (*group b*). Four of the patients in *group a* were men and 10 were women; 16 of the patients in *group b* were men and 11 were women. These data definitely show that the incidence of diabetic retinopathy is higher in women than in men The onset of the disease occurred in most of these patients between the ages of 35 and 54 years. Familial occurrence of diabetes mellitus was found more frequently among the patients with retinopathy than among those without retinopathy. Only 2 of the 14 patients in *group a* were obese, as compared to 12 of the 27 patients in *group b*. Most of the patients with retinopathy had not received adequate insulin therapy and had not kept to their diet. Half of the patients with retinopathy had complications such as severe glycosuria and hypoglycosuria. Only one third of the patients without retinopathy had such complications. Arteriosclerosis of the brain, the coronary arteries and of the extremities was observed in 10 of the 14 patients in *group a*, but only in 12 of the 27 patients in *group b*.

The primary role of the vascular disease in the diabetic changes of the eye is emphasized. Impairment of vessels frequently begins in the retina and this is of great significance for the evaluation of the general condition. The diabetic retinopathy is as a rule progressive. No therapy is known as yet which may definitely prevent this process or which may cause its regression. Insulin has a favorable influence on the metabolism, but can not prevent the developmens of vascular changes; the vascular disease may, however, have a better prognosit in these patients who are receiving adequate insulin treatment.

Comment: This review of 101 diabetic patients provides data in general agreement with many of the larger series in the literature. Thus, retinopathy was noted in 22 patients and was related to the duration of the diabetes; it was more common in women; the retinopathy group had a higher incidence of poor control and other vascular complications; and no specific therapy was found effective.

BERNARD BECKER

AN INTRAFAMILIAL EPIDEMIC OF PHARYNGOCONJUNCTIVAL FEVER

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A.M.A. Arch. Int. Med., 1957, *99:* 70–73

Pharyngoconjunctival fever has recently been recognized as a specific viral disease entity characterized by fever, pharyngitis, and conjunctivitis occurring singly or in combination, in epidemic or sporadic form. Virus-isolation studies and the subsequent development and application of APC group-specific complement-fixation and type-specific neutralization tests have shown that APC Type 3 virus is the etiologic agent. Epidemics have been reported from widely separated areas, but since this condition may be confused with a variety of other infections or may be mild enough not to require the services of a physician, many cases are probably not recognized or reported. The present study is a description of the disease as it appeared in a family of seven.

The intrafamilial epidemic was brought to our attention when a 12-year-old white boy was admitted to the Ohio State University Hospital because of a six-day illness characterized by pharyngitis, unilateral conjunctivitis, and fever which had not responded to a variety of antibiotics. A tentative diagnosis of pharyngoconjunctival fever made at this time was confirmed by virus-isolation and serologic studies. His condition improved progressively on purely symptomatic treatment and modified bed rest. He was free from fever two days after admission and was discharged feeling well on the fifth hospital day.

Since the family history revealed the fact that six of the seven members had recently been or were presently ill, it was decided to study the entire family from the clinical and laboratory aspects. The first member of the family to become ill was the patient's youngest sibling, a one-year-old boy, in whom rhinitis and bilateral conjunctivitis had developed abruptly about 8 days before the patient fell ill. The other members of the family were a 14-year-old girl, an 11-year-old boy, the parents, aged 37 and 35, and a 2-year-old boy who was not observed to be clinically ill during the period of illness of the other members of the family or in the following six months. APC virus, Type 3, was isolated from three of the seven during their acute illness, and a significant rise in serologic titers was demonstrated in these three and in the one-year-old boy who was well when examined but who had previously had the typical clinical symptoms of pharyngoconjunctival fever. Thus four of the seven members of the family were proved to have had pharyngoconjunctival fever. The parents, on the other hand, did not have symptoms of the same type or severity as those of the children; they failed to yield virus in HeLa cell culture, and showed no significant serologic titers. Their clinical signs, too, failed to fit the pattern of pharyngoconjunctival fever.

The clinical symptoms in the four children were strikingly similar, since all exhibited fever, conjunctivitis, pharyngitis, rhinitis, malaise, and cervical adenitis. Two of the four also had transient diarrhea. All responded to supportive therapy alone. The incubation period appeared to be between five and eight days. Since a carrier state of this virus has not been previously demonstrated, it is of interest to note that the virus was isolated only from the three acutely ill persons, from the conjunctiva, pharynx, and stool. One month later, after they had receovered, no virus could be isolated. The group-specific complement-fixation titers and the type-specific neutralization titers rose equally during the acute phase of the illness, but when the serologic studies were repeated about seven months later, no complement-fixing antibodies could be demonstrated, although the neutralization titers remained elevated. This observation suggests that the complement-fixation titer is transient in nature, while the neutralization titer is more persistent, a dissociation of serologic tests previously suggested by Heubner and his co-workers.

Comment: Early epidemiological studies of pharyngoconjunctival fever reported from Bethesda by Rowe and co-workers implicated Type 3 APC virus. It is now known from studies in California (Jawetz and co-workers) and Canada (Ormsby and co-workers) that symptoms of fever, pharyngitis and conjunctivitis can be caused by Types 2, 3, 4, 6, 7, and 9. It is quite possible that other adenovirus types will be found which cause similar symptoms.

The fall of complement fixing antibodies to zero after 7 months with persistence of high levels of specific neutralizing antibodies is interesting, since there is at this time no adequate data on the time that these antibodies persist in different individuals.

In our experience, adults seldom develop systemic manifestations with adenovirus infection, many exhibiting only a mild pharyngitis. When conjunctivitis occurs in adults, it is often fairly acute, and nebulous corneal opacities may be seen in the epithelium and stroma with the slit-lamp after the eighth or tenth days.

HUGH L. ORMSBY

THERAPEUTICS

HEPARIN IN SENILE MACULAR DEGENERATION

PRELIMINARY REPORT

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A.M.A. Arch Ophth., 1957, *57:* 190–199

Recent investigations indicate that one of the major factors in the development of atherosclerosis is the state of the circulating blood lipoproteins. Heparin apparently plays a major role in the degradation or interconversion of lipoproteins from larger to smaller molecules, during their serum transport phase. It has been postulated that endogenous heparin may be involved in a homeostatic mechanism controlling the serum transport phase of fat metabolism in a manner similar to insulin in carbohydrate metabolism. Because of its lipemia-clearing action heparin is being used as an antiatherogenic agent; this represents a new approach to the therapy of atherosclerosis. Engelberg has suggested that heparin might be of value in the treatment of eye conditions associated with arteriosclerosis.

In March, 1952, a study was begun to evaluate the effect of heparin on senile macular degeneration. The series consisted mainly of advanced cases in a routine office practice. Many of the patients had already lost the central vision in one eye, and in the other the vision had declined to 20/50 or less. In a large percentage of this group previous treatment with vasodilators, iodides, and other lipotropic factors, such as Methischol or sorethytan (20) monooleate (Sorlate) was without effect on the progressive loss of vision.

The dosage schedule arbitrarily used in this study was 100 mg. of the sodium salt of concentrated aqueous heparin (Lip-Hepin, Darwin Laboratories) intravenously, twice weekly. A series of 10 to 20 injections was given, followed by a 2–3 week rest interval. A few cases received 200 mg., subcutaneously in the fat tissue above the iliac crest, but since no better results were obtained, use of the lower intravenous dose was resumed. Clotting time determinations were omitted because the anticoagulant effect of this dose of intravenous heparin is known to be limited to less than 12 hr. The patients were cautioned to avoid bruising or cutting themselves, for instance in shaving, on the day of the injection and were warned not to have minor surgical procedures scheduled on that day. All subjects, including those with advanced cardiovascular disease with or without hypertension, tolerated the treatment very well. The only contraindications to heparin therapy are active internal ulceration, chronic liver disease, and a hemorrhagic diathesis.

TABLE 1

Results of Intravenous Heparin in Senile Macular Degeneration

Results*	No. of Cases
Markedly improved	9
Moderately improved	4
Slightly improved	4
Stationary	3
Worse	3
Total	23

* Grading of improvement: I. Markedly improved—final visual acuity 20/40 or better. II. Moderately improved—final V. A. 20/70-20/40 and an improvement of at least one line. III. Slightly improved—final V. A. less than 20/70 or an improvement of less than one line. IV. Stationary—no improvement, but no decrease of vision. V. Worse—V. A. became worse during therapy.

TABLE 2

Response of Various Types of Senile Macular Degeneration to Intravenous Heparin

Predominant Macular Lesion	Marked Improvement	Moderate Improvement	Slight Improvement	Stationary	Worse
Disciform (12 cases)	6	3	1	0	2
Arteriosclerotic (10 cases)	2	1	3	3	1
Cystoid (1 case)	1				

No untoward reactions were noted in more than 1000 intravenous injections of heparin. Two patients complained of becoming very "jittery," and one of them refused further treatment because of this unpleasant sensation. These observations are in accord with the common experience that intravenous heparin is the safest of all anticoagulants. Nevertheless, an ampule of protamine was kept handy for intravenous administration as a heparin antagonist, but in this series no occasion arose for its use. The absence of untoward side effects may be partially attributed to the selection of colorless concentrated (200 mg./cc.) aqueous heparin; the reprocessing necessary for this concentration results in a highly refined product.

The results are summarized in Table 1 and 2.

In this series the cases with disciform macular degeneration, which usually causes the most rapid and profound loss of central vision, showed the best response. A definite improvement and a delay in progress were also observed in the arteriosclerotic type of macular degeneration (Haab's senile macular degeneration).

Comment: This paper is quite timely. It is only a preliminary report and a larger series may fail to substantiate these initial results obtained in only 23 patients. However, in a recent survey by Sorsby, diseases of the macula were found to be the third largest cause of loss of vision—second only to cataracts and glaucoma in patients with advancing age. Up to the present, there has been no satisfactory therapy.

Most of these macular lesions are of unknown etiology. They are thought to be due to

a disturbance in circulation. It is well known that the circulation in the macula is particularly vulnerable. A good portion of the nutrition of the macula is obtained by way of the choroid. However, the foveal region and the immediate vicinity is entirely avascular. There are numerous capillaries in the surrounding area, but these are supplied by arterioles which are quite a distance away. The nutritional requirements are great and the blood supply scanty in view of the great number of neuronal elements in this small area. As noted by Nichols in 1956, the nutritional reserve in this area must be relatively small. Any reduction in minute volume of the blood flow will have a more severe effect here than in other parts of the retina. Perhaps the essential circulatory disturbance is the slowing of the capillary blood flow induced by narrowing of the arterioles. This narrowing can come about by sclerosis or spasm, or a combination of the two. The dysfunction may occur in the retinal or choroidal circulation, or in both. If we are to overcome this disease, it is essential that measures to improve the circulation of the choroid and retina be found. Studies with radioactive (tagged) red blood cells such as employed by Bettman, scleral window techniques, thermocouples to measure heat changes, and plastic injection methods as well as others have been employed to evaluate the influence of various vasodilators and other drugs which might improve the local circulation. Studies of this sort will give us information which may be helpful in the therapy of this ocular disease.

With the great interest shown in the conditions that induce athero- and arteriolarsclerosis, it is likely that a new approach to the therapy of circulatory diseases in the eye will develop. Controversy exists among those individuals interested in the therapy of atherosclerosis as to the value of diet, limitation of fat intake, the influence of agents such as sitosterol, so-called lipotropic agents such as lethcitin, methionine, choline inositol, estrogens and nicotinic acid as well as heparin. All of these methods or agents have been shown to have some influence on the lipids—their quantity and physical structure in the blood stream. Ophthalmologists can wait until other investigators have shown the merits of these agents on longevity and on the incidence of atherosclerosis before trying them for ocular disease processes, or we can contribute information now. Studies such as that done by Dr. Rome are in the right direction even if they are not adequately controlled and do not provide the final answer. The problem is not simple as attested by our failure to date to arrive at satisfactory therapy but, as more investigators enter the field, it is likely that at least some of our present macular disease conditions will be helped.

IRVING H. LEOPOLD

TREATMENT OF TEMPORAL ARTERITIS WITH ADRENAL CORTICOSTEROIDS

RESULTS IN FIFTY-FIVE CASES IN WHICH LESION WAS PROVED AT BIOPSY

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During the past six years, a number of patients with temporal arteritis that was proved by biopsy have been treated with adrenal corticosteroids at the Mayo Clinic. Most patients received cortisone, either parenterally or orally, but a few patients seen more recently received prednisone.

Despite intensive study, the causation of the disease remains unknown, and little has been added to the first description of temporal arteritis except in three aspects. First, it has become apparent that the arteritis may not be confined to the temporal or even to the cranial arteries. Lesions identical to those seen in the temporal arteries have been found in the aorta, carotid and pulmonary arteries, and in other peripheral and visceral arteries.

Second, it has been recognized that temporal arteritis is not an entirely benign condition, for there have been reports of deaths occurring during the course of the disease. Because the disease affects the elderly, and because it frequently is difficult if not impossible to determine the exact cause of death, there is no general agreement as to the true mortality rate of the disease. There is widespread agreement, however, concerning the frequency and seriousness of the most common and most severe feature of temporal arteritis, aside from the involvement of the temporal arteries themselves; namely, involvement of the visual apparatus, leading in all too many cases to permanent blindness.

Third, some progress has been made in the methods of treatment of this disease. It was recognized, in the early days of the treatment of temporal arteritis, that sectioning of the involved artery for biopsy frequently produced relief of the head pain. On the basis of this observation, injection of procaine hydrochloride along the course of the involved temporal artery has been tried, and striking relief of pain has been reported to follow it. Benefit also has been reported from the intravenous administration of histamine and from the use of chlortetracycline. For the most part, however, treatment remained mainly supportive and nonspecific. With the advent of the adrenal corticosteroids, a new approach to the treatment of temporal arteritis was possible. Since the first trial of cortisone against this disease, evidence has been accumulating that cortisone and related steroids exert a favorable effect upon the signs and symptoms of temporal arteritis, and it appears that at present the use of these hormones is the treatment of choice.

In the present series of 55 patients, the clinical diagnosis of temporal arteritis was confirmed in every case by microscopic examination of a section of tissue rom one of the superficial cranial arteries. There were 28 men and 27 women. The oldest patient was 83 years old and the youngest was 60 years old. All sections for biopsy were taken with the use of local anesthesia. Whenever possible, the biopsy specimen was taken from a site where the artery appeared abnormal or was abnormal to palpation. In some instances, the first frozen section studied at the time of biopsy indicated either that the artery was normal or that the results were inconclusive. In such cases, study of another section taken further along the course of the artery disclosed the typical pathological picture of temporal arteritis, demonstrating the frequently spotty arterial involvement in this disease. For this reason, repeated biopsy specimens always should be obtained when the presence of the disease is strongly suspected and results of the first biopsy are negative.

Cortisone therapy was begun as soon as the diagnosis was suspected. Previous experience has shown that it is neither necessary nor advisable to withhold

cortisone therapy until biopsy has been done. Usually, 300 mg. of cortisone was given intramuscularly on the first day of treatment, followed by 150 to 200 mg. injected intramuscularly daily thereafter, either in one injection or in divided doses every 12 hr. In some cases, treatment was continued by the intramuscular route, but in the majority of instances the mode of administration was changed to the oral route after subsidence of symptoms and decrease of the erythrocyte sedimentation rate to normal or nearly normal. When the oral route was used, the same total daily dose of cortisone was administered, but it was given in fractions every 4 to 6 hr. Whenever possible, cortisone therapy was continued, with daily doses of 150–200 mg. for 6 weeks. At the end of this period, the daily dose of cortisone was altered by decrements of 12.5 to 25 mg. every 3–4 days, provided the clinical progress of the patient was satisfactory and the erythrocyte sedimentation rate remained within normal or nearly normal limits. When the total daily dose was reduced to 12.5 mg., administration of the drug was discontinued. A few patients were treated entirely with orally administered cortisone in the same dosage as previously described. Three patients were treated with prednisone, the dosage beginning with 75 mg. the first day and then continuing with 50 mg. daily in divided doses every 4 to 6 hr. for 6 weeks. At the end of this time, the total daily dose was altered by decrements of 2.5 mg. every 3 or 4 days until administration of the drug could be discontinued.

Thirty-five of the 55 patients had some type of ocular involvement, as indicated in the history or disclosed by examination. These lesions are listed in Table 1. The occlusions of tributary retinal veins that were present in two patients and the bilateral macular degeneration noted in one patient probably were not definitely related to the temporal arteritis. In the remaining 32 patients (58.2 per cent of the total group), the ocular involvements seemed to be definitely parts of the syndrome of temporal arteritis. In 21 of these (or 38.2 per cent of the group of 55), there was loss of vision of varying degree. The most common

TABLE 1

Ocular Involvement in Fifty-five Cases of Temporal Arteritis

Ocular Involvement	No. of Patients
Due to temporal arteritis	
Ischemic optic neuritis	18
Retrobulbar neuritis	1
Optic atrophy	2
Toxic retinopathy	2
Ocular-muscle paresis	2
Transient amaurosis without permanent visual loss	7
Total	32
Not due to temporal arteritis	
Occlusion of retinal tributary venule	2
Macular degeneration	1
Total	3

cause of the loss of vision was ischemic optic neuritis, which was present in 18 patients. The optic neuritis was of the retrobulbar type in 1 patient. Optic atrophy secondary to optic or retrobulbar optic neuritis was noted at the time of the first examination in 2 patients. In 20 of the 21 patients, objective loss of vision was present at the time of admission; in 1 patient the onset of visual loss occurred 7 days after treatment with cortisone was begun. One other patient who could see only movements of the fingers with his left eye on admission lost the remaining vision in this eye after 10 days of treatment with cortisone.

In the group of patients treated with adrenal corticosteroids, the number of those bilaterally blind at the time of dismissal was no greater than the number of those bilaterally blind at the time of admission, and there were only 2 additional blind eyes, an increase of 12.5 per cent in respect to blind eyes. In contrast, in the group seen prior to the introduction of steroid therapy there was a threefold increase in the number of patients with bilateral blindness during the period of treatment and a 50 per cent increase in the number of blind eyes, from 16 to 24, in the course of treatment. Among patients seen before hormone therapy became available, 5 who were blind in one eye at the time of admission became blind in the remaining eye while under observation. There were no similar occurrences among those patients receiving hormone therapy. On the basis of the findings in 250 cases reported in the literature, it might be expected that bilateral blindness would develop in 22 per cent of cases of temporal arteritis. It occurred in 17 per cent of the Mayo Clinic patients not treated with cortisone and in only 9 per cent of those treated with adrenal corticosteroids.

All 55 patients in the current series were examined funduscopically at least once, and those who had visual symptoms received many such examinations. Visible edema of the optic disks was present in 18 of the 21 patients who had loss of vision, and pallor of the disks was present in the other 3. Loss of vision in all cases probably was due to extreme narrowing of the lumens of the ophthalmic or central retinal arteries. This does not necessarily mean that thrombosis or complete occlusion of the vessels had occurred, but it does mean that narrowing was sufficient to cause anoxic damage to the optic nerve fibers.

Among the 21 patients who had sustained permanent loss of vision, there were some in whom transient obscuration of vision of short duration had occurred in one eye or both eyes prior to onset of the persistent loss. Similar episodes of transient amaurosis had occurred in seven additional patients before treatment was started; permanent loss of vision did not develop in any of these patients. Such episodes may result from arterial spasm or transient circulatory insufficiency in the retina secondary to lesion in the internal carotid as well as in the ophthalmic or central retinal arteries.

The so-called toxic cotton-wool patches seen in 2 of the patients in this series probably result similarly from insufficient blood supply to the retina, since they were present also in the second eye of 1 of the patients who had unilateral loss of vision associated with ischemic edema of the optic disk.

Involvement of the blood supply to the extraocular muscles also seems to be a part of the syndrome of temporal arteritis, for several of the patients complained of more-or-less transient episodes of diplopia, and definite, objective

disturbances of ocular rotation were noted in two cases. It seems probable that ischemia of the extraocular muscles may result from arteric involvement, either of the ophthalmic artery itself or of its branches to individual muscles. The diplopia cleared rapidly under treatment in each instance.

In general, ocular symptoms began within 3 to 6 weeks after the beginning of headache and a somewhat shorter interval after the appearance of induration and hypersensitivity of the temporal arteries. However, some patients in this series had both headache and prominent, indurated, hypersensitive temporal arteries and at no time had any ocular symptoms. In some instances, visual loss occurred within a month of the appearance of such vague generalized symptoms as fever, malaise, and aching of muscles.

In the present study, we were unable to establish any credible correlation between the presence or absence of a pulse in the involved temporal artery and visual loss on the same side when the visual loss was unilateral. The occurrence of blindness did not correlate well with the severity of temporal artery involvement. There was some tendency for the loss of vision to occur on the side of the more severely involved temporal artery when both arteries were involved. The more severely involved temporal arteries tended to be more painful. Visual loss also occurred in both eyes when headache was unilateral. Finally, a number of patients had diplopia or transient amaurosis, even in repeated incidents, without the development of any permanent visual loss.

It is apparent, then, that it is unwise to attempt to select only certain patients with temporal arteritis for hormonal treatment. The present policy at the Mayo Clinic is to begin to treat immediately all patients suspected of having temporal arteritis with either cortisone or one of the related adrenal corticosteroids. In fact, treatment is begun prior to biopsy, if the latter procedure involves any delay. We prefer the intramuscular route of administration of cortisone for the first week or so of treatment because of the sustained high levels that it produces. If results of adequate biopsy prove negative, treatment can be interrupted with no harm having been done. At the present state of our knowledge of temporal arteritis, the foregoing seems to be the soundest approach to the problem.

Comment: Temporal arteritis produced ocular manifestations in 55 patients studied by this group. It is a self-limited and benign condition except for its ocular involvement. Visual loss is usually due to involvement of the optic nerve. This may be as an optic neuritis, retrobulbar neuritis, or eventually an optic atrophy. Occasionally one sees retinopathy and occasionally transient obscurations of vision. Therapy to date has been directed toward relief of symptoms by excision of portions of the involved artery, by injection of procaine along the course of the involved temporal artery, or by the intravenous administration of histamine. Anticoagulants have been employed as well as stellate ganglion blocks and vasodilating agents. None of these measures have resulted in any significant reduction of visual loss.

Steroids have been shown in many reports to produce definite relief of symptoms. The present study has demonstrated that steroids will relieve the symptoms such as headache, malaise and generalized muscle pains but will not restore visual acuity which has been lost. According to the data, steroids administered in adequate dosage will block progression of the ocular manifestations in the majority of patients so treated. The combina-

tion of anticoagulants and steroids or other therapeutic measures along with steroids were not evaluated in this present study. Anticoagulants might prevent the development of thrombi or extension of existing thrombi which would not be influenced significantly by steroid therapy. Apparently steroids will control the arteritis as long as it persists and in this way may safeguard the visual acuity. If steroid therapy is stopped early, there may be a recurrence of the patient's symptoms as well as progression of the ocular signs. On the basis of this study, steroids should be used for all patients with temporal arteritis, particularly those in whom ocular manifestations have not yet appeared. These hormonal agents may prevent the development of ocular manifestations in those who have not already suffered from them or guard the patient against further extension of existing ophthalmic lesions. Other therapeutic measures will have to be found which, along with steroid therapy, might facilitate circulation in the diseased vessels such as the ophthalmic artery, the retinal vessels, and the small nutrient vessels supplying the optic nerve.

IRVING H. LEOPOLD

DIAGNOSIS

RADIOACTIVE PHOSPHORUS IN DIFFERENTIAL DIAGNOSIS OF OCULAR TUMORS

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The differential diagnosis between benign and malignant lesions within the eye is complicated by the fact that many intraocular lesions cannot be subjected to biopsy without irreparable injury to visual function. In ophthalmology, as in other fields, the possible value of radioisotopes in the diagnosis and treatment of malignant lesions has been extensively studied in recent years, with the result that radiophosphorus, P^{32}, has emerged as the isotope of choice in ocular investigation. The excessive uptake of this substance by malignant tissue in the eye has been described by many authors. The predominant value of radiophosphorus in ophthalmology, however, lies in the fact that the radiation emitted is beta radiation. All of this radiation will be effectively stopped by about 8 mm. of tissue and there will therefore be no masking effect from more remote tissues. The physiologic, anatomical, and physical difficulties that may be met with in counting P^{32} around the eye make the technique of counting a matter of great importance; both the position of the counter and its inclination may have a critical effect on the results. Since it is generally agreed that the closer one can place a counting device to the suspected area the more accurate will be the result, it seems that the test is on a sounder basis in the case of the more easily accessible anterior lesions than in that of the remote posterior lesions. The P^{32}

emission of anterior lesions is counted with a small Geiger-Muller tube with an end-window placed directly over the lesion. For posterior counting, curved Geiger-Muller tubes and curved scintillation counters have been designed.

In the investigation of this subject made at the University of Michigan from July, 1954, to May, 1956, certain technical standards were found to be advisable. The average adult patient is given 500 μc. of P^{32} intravenously. For children the dose is adjusted downward on a weight basis. Experience showed that the only reproducible results were obtained in delayed counts, and the opinion now held is that a single evaluation at about 48 hr. after injection gives the most significant results. It is important to recognize the fact that many nonmalignant lesions will give an excessive count a few hours after the injection, but that this count will subsequently decline. For reasons that cannot be explained, counts may vary enormously under apparently standard counting conditions. Consequently, enough counts (the number will vary with the individual case) must be made to establish a definite trend for each patient. The establishment of such a trend may be quite a time consuming procedure. A standard must also be created for each patient. In some cases the entire affected eye will show an excess over the nonaffected eye, so that the nonaffected eye will be the standard. In other cases, particularly with small lesions, such as localized iris lesions, the affected area may show an excess over the rest of the eye, which then becomes the standard. In cases of suspected bilateral disease, or when the patient has only one eye, it has been suggested that a neutral tissue such as the ear lobe be used as a control area. The advisability of this procedure, however, may be questioned, because very high uptakes have been recorded from such normal vascular tissues as the tongue. A redemonstrable definite excess uptake of 30 per cent in 48 hr. has been used as a criterion of positivity in this study.

The procedure produces very little irritation of the eyes. A drop of sulfacetamide U.S.P. (Sulfamyd) 30 per cent is routinely instilled at the end of the test. General anesthesia is suggested for young children. Posterior counts are regarded as operative procedures and the patient is prepared and draped in the usual operative fashion. No complications or incidents occurred in any of the 80 isotope countings on which this report is based. Only the cases (24) in which pathological proof of the malignancy of the lesion was obtained have been considered in evaluating the findings. This, of course, weights the report in one respect, since it is only the most suspicious cases that come to operation. Even so, there were three false negative results. In one of these cases of proved malignancy, the results were negative with both anterior and posterior counts, made 10 months apart. In connection with another case, in which the results were negative with an anterior count and positive with a posterior count, it may be noted that reports of false positive results, especially in inflammatory disease, are also to be found in the literature.

Thus, although the differential uptake of P^{32} by malignant ocular tissue may be definitely helpful in the diagnosis of ocular malignancy, the entire clinical picture must be taken into consideration and the final decision must be based on clinical judgment. Moreover, in view of the lack of knowledge of the long-term

results of body radiation, the use of isotopes for diagnostic study must be undertaken cautiously. They should not be used when other methods of investigation, such as biopsy or excision, can be safely tried.

Comment: Ophthalmologists are well aware of the difficulty encountered at times in distinguishing between a benign and a malignant intraocular lesion. Radioactive isotopes have been employed in an effort to aid in this diagnosis. A number of institutions and laboratories are working on this problem. From the data which is accumulating rapidly, it appears that the differential uptake of radioactive phosphorus by malignant ocular tissues can be a definite adjunct in making the difficult diagnosis of intraocular malignancy. There are definite criteria and techniques which must be followed, as the test is not foolproof. Great effort must be made to hold the counter properly, that the areas of the external rectus muscle be avoided, and that one take sufficient counts in each area so that a definite trend in the counts for these positions can be established. Although comparisons may be made between comparable areas in the two eyes, this is not sufficient to allow one to decide between a positive and negative result. Sometimes the involved suspected area will give a much higher count than other areas in the same eye and this may be more significant than the results of the comparison between the values obtained in comparable areas in the two eyes.

Dr. Shapiro used, as a criteria of positivity, repeatable definite excess uptake of 30 per cent in 48 hr. Terner, Leopold and Eisenberg used a reading at 1 and 24 hr. and considered an initial count above 30 per cent as significant but did not make a positive diagnosis unless the 24 hr. count was greater than the 1 hr. count. They tried 48 hr. counts and found the readings were so low that they were running in the range where they were not felt to be reliable. As experience is accumulated, it may become apparent that a 30 per cent difference is too great for a positive test and that this value should be lowered. For the sake of gathering clinical information, it would appear that readings at 1, 24 and 48 hr. might allow accumulation of data which, when reviewed at a later date, would definitely substantiate the necessity of both readings or only one. The reasons that Terner, Leopold and Eisenberg used a 1, 24 and 48 hr. count was to establish a curve on the basis that malignancy might retain the radioactive phosphorus for a longer period of time than the inflammatory tissue. This appears to be the case in ocular tumors on the data obtained to date.

Posterior probes add other problems to the technique. As it is so important to apply the probe in the proper position, it is difficult to obtain this where the probe is slipped under tissues so that its head cannot be under direct observation in which case it is very easy to err by tilting the head or by allowing some extraocular tissue to get between the probe and the sclera. Posterior probe techniques would be more reliable if the site at which the probe is to be applied can be under direct observation at all times. It might be more reliable if comparable areas of the two eyes could be compared. This is rarely possible. Much more experience is required before the posterior probe can reach the present status of the anterior probe. Perhaps the value of the posterior probe will best be worked out in the experimental animal. There is no doubt that this is a definite adjunct.

It is evident from the accumulating data in various laboratories and hospitals, that the use of radioactive phosphorus in proper fashion can be of definite help in the differential diagnosis of intraocular malignancy. As Dr. Shapiro said "However, the entire clinical picture and judgment is the final determining criterion and the test is considered as an adjunct only."

IRVING H. LEOPOLD

Basic Sciences

BIOCHEMISTRY

ACTION OF DIAMOX AND AMMONIUM CHLORIDE ON FORMATION OF AQUEOUS HUMOR

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The lowering of the intraocular pressure by Diamox has led to the suggestion that the enzyme carbonic anhydrase is essential to the formation of the aqueous humor, and this idea has found expression in the hypothesis that the reduction of the intraocular pressure by Diamox is due to an inhibition of secretion across the blood-aqueous barrier. This view had its origin in the studies of Friedenwald and Stiehler on the transfer of acidic and basic dyes across the epithelial layers of the ciliary processes. Friedenwald suggested that hydroxyl ions were secreted into the aqueous humor, and that an excess of bicarbonate was produced from the reaction of the hydroxyl ions with carbonic acid. This view was supported by Kinsey who observed in rabbits that the concentrations of hydroxyl and bicarbonate ions in the aqueous humor exceeded those in the plasma. The participation of carbonic anhydrase in this secretory activity was supported by the reports of the presence of the enzyme in extracts of the iris and the ciliary processes.

There is general agreement that the reduction in the intraocular pressure is accompanied by a decreased rate of formation of aqueous humor, but the means by which this is brought about is still unresolved. Becker and Becker and Constant reported that their experimental results were consistent with the view that Diamox lowers the intraocular pressure by directly inhibiting the secretion of aqueous humor and in particular the transfer of excess bicarbonate into the aqueous humor. However, evidence that the ratio of the concentrations of bicarbonate between the aqueous humor and the blood was unchanged in animals given Diamox, in spite of the absolute decrease in the concentrations, led the present authors to question whether the production of excess bicarbonate in the eye in fact depends on a secretory mechanism involving carbonic anhydrase.

In the present study three aspects of this problem have been considered. First, the pH and the distribution of bicarbonate ions between the blood and the aqueous humor before and after the administration of Diamox have been determined. In particular, attention has been focused on possible differences between the composition of the fluids in transient and steady-state conditions. This was

undertaken in view of the rapid decrease in the intraocular pressure that takes place immediately after giving Diamox. Similar studies were made on animals with the renal arteries tied off and on animals given ammonium chloride in view of the interesting observations of Becker that neither the administration of ammonium chloride nor nephrectomy made animals unresponsive to Diamox.

The second aspect of the problem concerns the effect of Diamox and ammonium chloride on the rate of formation of aqueous humor. For this purpose, fluorescein has been used as the test substance, and the concentration of fluorescein in the anterior chamber has been continuously recorded.

The third aspect deals with the changes in the intraocular pressure in animals given Diamox or ammonium chloride during the period leading to a new condition of steady-state. This has assumed an increasing importance in view of observations that the effect of Diamox on the rate of formation of aqueous humor and distribution of bicarbonate ions across the blood-aqueous barrier was minimal in conditions of steady-state.

In assessing how Diamox influences the composition of the aqueous humor and intraocular dynamics several observations merit special mention. First, Diamox caused a reduction in pH and also in the concentrations of bicarbonate in the aqueous humor and the blood, but only a temporary reduction in the ratio of the concentrations of bicarbonate between the aqueous humor and the blood. Secondly, there was a rapid but only temporary decrease in the rate of flow of the aqueous humor. Thirdly, Diamox neither inhibited the secretion of ascorbic acid across the blood-aqueous barrier nor significantly affected the distribution of sodium between the two fluids. Lastly, there was a rapid and significant fall in the intraocular pressure followed by a partial or complete recovery. It would seem to follow that, in the continued presence of Diamox, there is little or no effect on the intraocular dynamics of the normal rabbit eye. At the same time, in confirmation of previous investigations, our experimental results show that Diamox can cause transient changes in the intraocular pressure and in the formation of the aqueous humor. For this reason, the animals employed in this study could not be considered resistant to the action of Diamox.

Diamox caused a temporary disturbance of the normal distribution ratio for bicarbonate, the excess of both hydroxyl and bicarbonate ions in conditions of steady-state were proportionately the same as in normal untreated rabbits. It is therefore evident that Diamox, even though it may completely inhibit the carbonic anhydrase activity in the ciliary processes does not alter the normal distribution ratios of these ions. Consequently, it is unlikely that carbonic anhydrase activity in the eye is essential to the accumulation of excess bicarbonate in the aqueous humor.

The analyses of the sodium content of the aqueous humor show that the marked loss of bicarbonate immediately after giving Diamox is not accompanied by an equivalent decrease in the concentration of the main cation, sodium. It would seem that there was no marked reduction in the rate of transfer of sodium into the eye either during this period or in conditions approaching steady-state. The constancy of the steady-state ratios for the sodium, hydroxyl, and bicarbon-

ate ions lends support to the experimental evidence that the intraocular dynamics remain essentially unchanged after the administration of Diamox.

The transfer of ascorbic acid across the blood-aqueous barrier was studied in the belief that if Diamox affected the secretory mechanism in the manner postulated by Friedenwald, the transfer of ascorbic acid would presumably also be modified. Ascorbic acid is the only compound which is universally agreed to be secreted across the ciliary processes, and to it has been ascribed a cardinal role in the secretory mechanism. It is therefore of some significance that the transfer of this compound across the blood-aqueous barrier underwent no significant change in the presence of Diamox. It is true that the small increase in the concentration of ascorbic acid in the aqueous humor of animals given Diamox three hours previously is consistent with an increase in the rate of secretion; but, on the other hand, it may be more simply ascribed to the transient decrease in the rate of flow of the aqueous humor during the first 1 or 2 hr.

There is general agreement that fluorescein can be used as a test substance to measure relative changes in the rate of flow or in the formation of the aqueous humor. The experimental results in this paper showed that the time taken for fluorescein to pass from the bloodstream and into the anterior chamber via the posterior chamber increased by approximately 50 per cent, fourteen minutes after the administration of Diamox, and that this increase in the time of flow remained high for at least 1 to 2 hr. Subsequently, however, there was a return of the flow-time to normal in spite of the administration of further amounts of Diamox. The changes in the rate of flow of the aqueous humor after the administration of Diamox is of interest in that the initial decrease in the rate of flow occurred at the same time as the loss of bicarbonate in the aqueous humor. Furthermore, the recovery of flow to normal was concurrent with the return of the bicarbonate distribution ratio to normal. Presumably the action of Diamox in decreasing the rate of flow of the aqueous humor is associated with a disturbance of the normal osmotic balance between the aqueous humor and the blood, and these results are consistent with the view that the loss of bicarbonate in the aqueous humor was responsible for the temporarily decreased rate of formation.

The conclusion emerging from these studies—that the intraocular dynamics of the normal eye are almost, if not completely, undisturbed by Diamox in conditions of steady-state—is not inconsistent with the well-proven fact that, in similar conditions, the intraocular pressure is decreased and controlled in the glaucomatous eye. It is reasonable to assume that the immediate action of Diamox on the body is basically the same, and that the essential difference in the final equilibrium is determined by the different properties of the hypertensive eye. Theoretically, there are several factors which could make the eye with a high intraocular tension react more dramatically than the normal eye. First, there is the obvious reason that a given change in flow will lead to a greater absolute fall in the intraocular pressure if the initial pressure is high. Secondly, there is the possibility that homeostatic mechanisms are operating in the eye with a normal intraocular pressure and not in the eye with a pressure above a certain critical level. In this case, Diamox may reduce the pressure sufficiently

to the level at which the homeostatic mechanism acts. Thirdly, it is possible that the relative contributions of filtration and osmotic pressures in the maintenance of the flow of the aqueous humor are not the same in the two cases. In this event Diamox could affect the rate of formation of the aqueous humor in the normal and abnormal eye disproportionately.

In bringing together these findings on normal and glaucomatous eyes, the evidence is consistent with the view that Diamox modified the osmotic balance between the blood and the aqueous humor independently of its renal action. The mechanism remains unsolved, but would appear to be related to an increased acidity in the eye. In animals, however, this increased acidity relative to that of the blood was only temporary. This could have been due to a disproportionate inhibition of carbonic anhydrase activity in different regions of the eye through a slow penetration of Diamox, or it could have reflected the ability of the eye to reassert the normal concentration ratios of hydroxyl and bicarbonate ions between the aqueous humor and the blood. Apart from the changes in the concentration of bicarbonate in the aqueous humor immediately after giving Diamox, no evidence has been found to support the view that Diamox inhibits the secretion of bicarbonate into the eye. The possibility that Diamox directly or indirectly inhibits the active transport of some other ion such as sodium or chloride cannot be answered from this study.

Comment: For the clinician, the controversial problems of aqueous humor dynamics are difficult to weigh. However, some of the results are difficult even for the experts in this field. Following one of the meetings at which this paper was delivered, it was suggested that the points of agreement and disagreement in regard to the effects of Diamox be listed. It was found that there was greater agreement than had been anticipated, and in only one point was there definite disagreement. The points of agreement are that: 1) Diamox lowers the intraocular pressure, 2) Diamox decreases the rate of aqueous formation, 3) the Diamox effect is independent of the renal effect, 4) Diamox reduces the bicarbonate excess in rabbits' aqueous humor, 5) Diamox decreases the pH of aqueous humor slightly, and 6) ascorbate rises in the aqueous after Diamox.

The point of disagreement is in the bicarbonate ratios. Becker found that at the end of 6 hr. after Diamox administration the bicarbonate in the anterior and posterior aqueous was reduced but that there was *no* fall in the plasma bicarbonate. These experiments were done in nephrectonized animals. Langham found a fall not only in the aqueous but in the plasma. Unfortunately he did not consider posterior aqueous studies. Kinsey, in unpublished experiments (personal communication), found that five hours after the beginning of continuous administration of Diamox the anterior and posterior aqueous and plasma concentrations fell in non-nephrectonized rabbits. This indicates that Langham and Kinsey found the ratios undisturbed while Becker found only the plasma level unchanged.

In the discussion of analytical methods, Langham implies that one is wrong in using plasma as Becker did instead of whole blood to determine bicarbonate. Actually the effect of Diamox on possible inhibition of carbonic anhydrase in red blood cells suggests that this may not be the case and that serum should be used.

H. Saul Sugar

OPTICS

STEREOPSIS AND UNEQUAL LUMINOSITIES OF THE IMAGES IN THE TWO EYES

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The extent to which a difference in the luminosities of the images in the two eyes can affect binocular vision and, in particular, stereoscopic depth perception has interested research workers in vision for a long time. The most striking effect, of course, is the Pulfrich stereophenomenon, in which the stimulus object is in motion while the background is fixed. The bob of a swinging pendulum appears to move in a more or less elliptical path when the image of one eye is darkened by a filter. That an effect on the stereoscopic depth occurs with ordinary and static spatial configurations has been less certain. Verhoeff (1933) described his observations with a stereoscope in which he used equally inclined black lines on a white background as test targets and then darkened the image in one eye by a smoked glass or filter. When the absorption of the glass was of the order of from 80 to 95 per cent, depending on background illuminance (luminosity of the background was regarded as that of the image), he reported two effects: (1) The fused image appeared to deviate laterally toward the brighter image, and (2) the stereoscopic sagittal inclination of the line was reduced about one-third. The lateral deviation, which Verhoeff stated is proportional to the difference in the luminosities, and to the disparity, "has the effect of reducing the disparateness," and, therefore, the stereoscopic depth. "The phenomenon," he concluded, "occurs with any kind of disparate images." This concluding generality is hardly justified on the basis of introspective observations. Nevertheless, it has been accepted.

The experiments carried out by Verhoeff and later repeated by others, together with the conclusions arrived at, have an important bearing on the problem of the relationship between disparity and stereoscopic depth and on the problem of the stability of stereoscopic depth for given disparities between the images, implying as they do that the difference in luminosity of the images results in a decreased physiologic disparity between the images. The whole question has therefore been re-examined by means of three experimental arrangements in which it was possible to measure the amount of reduction, if any, that occurred.

The basic experiment was to determine the validity of stereoscopic perception of depth, and the stereoscopic acuity from the disparate images of a single stimulus, when a filter is placed before one eye so as to reduce the luminosity of one

of the disparate half-images. Three subjects, all of whom had had experience in stereoscopic observations, were used in this study. The instrument used was a modification of a haploscopic device. Data were obtained to determine (1) the disparity corresponding to the most probable position of a test line when it and the reference line appeared equally distant and (2) the stereoscopic acuity as neutral-tint filters of different light transmissions were used to change the luminosity of the image of the test line for one eye. Since the Verhoeff phenomenon is said to occur only when there is a disparity between the images of the test object, the data were obtained when the reference line was placed in front of (or behind) the plane of the fixation point, for in this position the images of the reference line would be disparate. If the test line was then set so as to appear at the same distance, its images would correspondingly be disparate. It must be remembered that only the disparate images of the test line and not the fixation point or the reference line are affected by the filters.

From the data so obtained, it must be concluded that a difference in the luminosities of disparate images themselves in the two eyes does not result in a decrease in stereoscopic depth. As long as the contours of the test object are perceptible, the stereoscopic depth is essentially the same.

The next step was to study the apparent inclination of a line, as in Verhoeff's experiment. In order to avoid the use of drawn figures to be observed in a stereoscope, an actual stimulus line consisting of a heavy white thread tautly stretched and mounted in a frame which could be inclined sagitally (fore and aft) in the median plane was set up. The degree of apparent inclination could also be measured by a test device consisting of two small white beads strung on a taut black silk thread. This second thread was invisible against the black background used for the second series of experiments, but the inclination of the line of the test beads could be adjusted by the subject by means of a hand wheel. The inclination of the stimulus line was set at some given angle, with the top either toward the subject or away from him. He was then asked to adjust the line of the two beads (1) so that they appeared parallel (sagittally) to the stimulus line and then (2) so that they appeared subjectively vertical also in the sense of a backward and forward inclination. The average of a series of settings for each of these two criteria was obtained as neutral-tint filters of various transmissions were inserted before one eye or the other to reduce the luminance of the retinal image of the stimulus line in that eye. Again the data obtained show that a change in the luminosity of the image in one eye did not result in a change in the physiologic disparity between the images. It was found, however, as one of the results of this study that decreasing the luminosity of the image in one eye does decrease the stimulus for cyclofusional movements.

In the first two sets of experiments, the adaptation levels of the two eyes had been kept the same. In the third set, the apparatus used (basically a haploscope with the same stimulus and test lines as before) was set up to duplicate the conditions of the original Verhoeff experiment, while at the same time providing for measurement of the apparent inclination of the perceived line in space and also or determination of the cyclotorsional positions of the eyes under the influence

of the declination of the images. As in the preceding experiments, it was found that a cyclotorsion does occur, with individual differences, and that its magnitude decreases as the luminosity difference between the two eyes increases. The data also showed that the apparent inclination of the fused stereoscopic images was unaffected by a decrease in the luminosity of the image in one eye; that is, there was no change in the physiologic disparity stimulus when the luminosities of the images in the two eyes were made unequal. The Verhoeff stereoscopic effect could not be verified.

From these three sets of experiments it seems clear that decreasing the luminosity of the image of one eye does not alter the physiologic disparity between the images of the two eyes and that the stereoscopic depth resulting therefrom is stable.

Comment: Ogle and Groth made a rather unrewarding choice in selecting this research problem. It is, in general, little rewarding to recheck the results of others and especially little seems to be accomplished in the public eye when the control study is negative, suggesting that some earlier published, and sometimes generally accepted, results are of little or questionable value or no value at all. This, however, is a rather unfair attitude toward research workers and their accomplishments.

It is no less important to clarify lazy concepts than to publish newly discovered phenomena; as a matter of fact, this study offers much more than the authors' modest summary of their own paper would suggest. Their results did more than "not verify the original observation" that "stereoscopic depth from static spatial line configurations was reduced when the image of one eye was darkened by a filter."

Their results prove the faultiness of a certain type of experiment, so common in the field of so-called psychophysics, and of experimental results purely based on introspective observation without offering anything quantitative to measure or to compare. Too often in such cases "when one attempts to measure the observed phenomena" one finds nothing to measure. It is this methodologic criticism of results, often called "classic" but in reality only dated, which gives this unusual paper its significance, in spite of the seeming "negativeness" of its results.

ARTHUR LINKSZ

IRIDECTOMY IN GLAUCOMA

A Study of the Glaucomatous Process

Albrecht von Graefe

Berlin, Germany

Archiv für Ophthalmologie, 1857, *3:* 456–560

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The incurability of glaucoma seems to be due to the fact that ocular changes are consecutive and originate from an extraocular source. The whole question of glaucoma therapy took on a different aspect, however, when I realized that the blindness was to be attributed not to changes in the optic nerve, but to an increase in intraocular pressure. The increased pressure is the main cause of the damage, particularly of the excavation of the optic nerve. As a curative measure I propose that by some means or other a lowering of intraocular pressure be effected.

All efforts to produce a rapid outflow of fluid from the eye by general measures failed. Finally, I experimented with repeated paracentesis which gave such startling results at first that I published them without hesitation (Arch. f. Ophth., 1855, *1*). Visual acuity was improved by the outflow of the turbid aqueous and its replacement by transparent fluid. The paracentesis had the great advantage of proving that many symptoms of glaucoma, such as the corneal anesthesia, depended on the rise of pressure. As a result of the paracentesis, I could distinguish the ecchymotic changes in the fundus in the early stages of the disease, since the refractive media cleared immediately. Unfortunately, however, the beneficial results proved only temporary in the vast majority of cases. In the few eyes which were improved by the operation, visual acuity was not greatly reduced by the inflammatory exudation, in spite of all the initial symptoms of acute glaucoma. In the other cases after a period of improvement of days, weeks and even months, deterioration began, not, as a rule, in the form of a violent inflammation, but as chronic glaucoma. Even when the improvement lasted longer than three months, an unfavorable prognosis could be given because of the gradual constriction of the visual field. I tried to combat these relapses, at first, by methodical repetition of the paracentesis, but each time the therapeutic effect became shorter in duration and finally the vision ceased to improve.

It was the use of iridectomy in ulcerations and infiltrations of the cornea which led me to the discovery of its pressure-reducing action. Operations for partial

staphyloma of the cornea and staphyloma of the sclera usually consisted of an attempt, first, to remove the staphyloma, then to form a new pupil, if this was needed. When I reversed this order for another purpose, I noticed that after an iridectomy the ectatic part frequently receded to the normal level of the cornea, and that the second operation was unnecessary. In fact I saw cases in which repeated attempts to correct the staphyloma failed until an iridectomy was performed.

Fortified by these facts and hypotheses I felt justified in performing an iridectomy in glaucoma. I knew the favorable effect of the operation on the choroidal circulation. Everything seemed to promise that the operation might have a physiologic and a therapeutic effect in lowering pressure. The first attempts varied extremely, since I had no criteria for the choice of cases or for the details of the operation. I began to use this method in June, 1856, and from that time applied it in cases of acute glaucoma. The immediate effect appeared favorable, but recalling my disappointment with paracentesis, I was extremely mistrustful. A continuous improvement became apparent, however, as the observations were prolonged. The signs of glaucoma gradually disappeared. After observing a few of the patients for more than a year and many of them for more than nine months, I believe the operation of iridectomy to be a curative measure to combat glaucoma.

Iridectomy In The Prodromal Stages of Glaucoma

It is not often that patients seek medical assistance when prodromal symptoms of glaucoma appear in the first eye affected; these are either overlooked or regarded as of little importance. On the other hand, it often happens that after the vision in one eye has been lost from glaucoma, the patient is alarmed by prodromal symptoms in the other eye. The question then arises as to whether one should await the distinct outbreak of the disease in the other eye or should he interfere during the prodromal stage. I hesitated a long time before doing the latter, because vision was still good intermittently, and because I lacked complete confidence in the procedure. As I gradually became bolder, I began to operate in a few cases during the prodromal period, and was entirely satisfied with the results. Loss of vision did not occur in a single case following iridectomy. The ciliary pain and colored halos disappeared. The periodic clouding of the aqueous also vanished and did not return. The anterior chamber appeared deeper than before. I could not decide whether or not a slight decrease in presbyopia occurred. In three of these cases, clouding of the vision had occurred rather frequently for several months before the operation. For this reason the effect seemed to be permanent. Visual acuity is as little influenced as is the accommodation by the presence of a moderately broad coloboma. Moreover, the possible small changes in this respect, contrasted with the certainty of complete blindness, are not worthy of consideration.

There cannot be any disadvantage in temporizing and in using internal medication. Any operation, however safe, may harm the patient accidentally or as a result of his disobedience. I usually advise patients in whom one eye is blinded from glaucoma and the other eye is threatened to submit to an operation when

the prodromal symptoms appear in the second eye, especially if diminution of vision occurs. One should not wait for a severe inflammatory attack. Even if an iridectomy affords complete relief from symptoms during the acute stage, the whole management of the patient at this time demands greater care and caution, and the operation itself is more painful. Massive retinal hemorrhages may occur making the restoration of vision slower. Changes in the iris, fixed pupils and paralysis of accommodation usually continue. The prodromal stage may never pass into the acute form but may develop gradually into the chronic form through the continuous protraction of the exacerbations.

Even when the prodromal symptoms have lasted a long time, iridectomy gives the same result. In this connection, I might mention a patient whom I treated for two years. One eye had been blinded by glaucoma and the second was in the prodromal stage. The periodic obscuration of vision became more frequent and more intense and I knew of no means to check the glaucomatous process. I gave, therefore, the most pessimistic prognosis and sent the patient home. About nine months ago one of my assistants, Dr. Alfred Graefe, performed an iridectomy on this patient, with splendid results. The reduction in visual acuity in the meantime, however, had become severe.

Iridectomy in the Acute Period of Inflammatory Glaucoma

My experiences are far more numerous in cases during the acute period of inflammatory glaucoma than in those during the prodromal stage. I operated more than twenty eyes shortly after the outbreak of the first marked inflammation which, in a few cases, was so severe that an operation seemed disastrous from the start.

I sought, at first, to alleviate the symptoms by antiphlogistics, opiates and similar treatment. I became convinced, however, that immediate iridectomy was necessary. Under these conditions every delay causes increased damage, and the surest help for the inflammation lies in the operation itself. After the operation not only did the symptoms improve without other means of treatment, but a rapid clearing of the refractive media occurred in every case. Seven days after the operation, the eyeground could be seen clearly with the ophthalmoscope. I thus ascertained the following facts about the process which later were of considerable aid:

1. The optic nerve is entirely normal after the first attack. Cupping or displacement of the vessels is not present, provided that chronic glaucoma has not preceded the attack but that the disease has occurred in a normal eye or after an intermittent prodromal period.

2. The same condition exists in respect to the arterial pulse.

3. The punctate hemorrhages in the retina are present constantly, but, undoubtedly, most of these occur after the operation.

4. In a careful observation of the equatorial region frequent choroidal hemorrhages are seen. These disappear quickly, however. It is not yet clear whether their inconstancy is not due entirely to the time of observation, since I have discovered them several times prior to operation.

Visual acuity as a rule improves immediately after the operation. This seems

to depend, as in the case of paracentesis, on the outflow of the turbid aqueous. The degree of improvement, however, is not considerable when compared with the subsequent improvement, which may be explained partially as the clearing of the ocular media. In my opinion, however, this improvement results more from the resumption of the retinal functions which have been depressed by the intraocular pressure.

The condition of the iris varies according to the degree of involvement. I have never seen a completely movable, normal iris once marked inflammation has occurred. Partial mobility is found frequently, but in the majority of cases the pupil remains completely paretic although not as dilated as before. Occasionally the pupil is somewhat narrower than normal, with due allowance for the coloboma. The irregular form and position of the pupil seldom disappears even if posterior synechia are not present. This may be attributed to an irregular distribution of the paralysis of the ciliary nerves. Hence, it is a question whether the permanence of the pupillary damage is due to structural changes in the iris itself or to changes in the ciliary nerves. It is difficult to decide this, but I am rather inclined to the first opinion. The iris never regains its normal appearance in well marked cases. An ashy gray discoloration remains, as well as an indistinctness of the trabeculae, either in spots or in large areas, especially toward the periphery. This fact, which affords ample evidence of the disease, is important in the later recognition of the case. The tension of the globe returns entirely to normal; in fact, in some cases the eyes seem a trifle softer after operation than before.

In all the cases in which operation was performed within two weeks after the beginning of the inflammation, a complete restoration of vision occurred. The patients in several of these cases seemed desperate, having lost every trace of the perception of light. It is hardly necessary to add that I offered them little hope. I merely undertook the operation because of the violent ciliary pain. The result, however, was truly astounding. For the last half year I have predicted the complete return of function, provided that less than two weeks have elapsed since the beginning of the inflammation and that some perception of light still exists. My early anxiety that the results might not be permanent gradually vanished. The visual field remained absolutely normal. Eccentric vision maintained its acuity once it had returned to the previous level. Not the slightest prodromal symptom recurred. The congestion of the subconjunctival vessels disappeared entirely; the anterior chamber became deeper and nothing betrayed an abnormal condition of the eye except the discoloration of the iris and the inactivity or paresis of the pupil. I cannot absolutely allay fear of a recurrence because of the short duration of my observations. It is certain, however, that a similar inhibition of the glaucomatous process has never occurred spontaneously or after any other form of treatment.

In spite of the surprising results of iridectomy shortly after the beginning of the inflammation, an exact analysis of the facts shows the correctness of the argument in favor of operating during the prodromal state. I would call special attention to the relative danger of the operation during the two periods. In the prodromal stage a chance accident seldom occurs even when the operation is not

performed correctly. In the acute period, on the other hand, with every precaution, the result may be disappointing because of retinal hemorrhages and other adverse conditions which may occur in isolated cases in spite of the greatest care. This can be decided only after comprehensive statistics are gathered.

Observation of these patients showed that iridectomy does not influence the second eye. Frequently the process starts in the second eye after the first has completely recovered. It can be said with certainty that the glaucomatous inflammation of the second eye does not arise sympathetically from the disease of the first eye.

Iridectomy in the Later Periods of Acute Glaucoma

Although the curative value of iridectomy is most marked in cases of short duration, it loses none of its importance in disease of longer standing. My observations in this group are even more numerous than in the others. Because of variability of the results, however, their final evaluation has been more difficult, and a continuation of these studies is necessary. The following is only a preliminary report:

1. A lapse of weeks or even months after the first glaucomatous attack does not prevent complete restoration of sight; this depends entirely on the characteristics of the individual case. Occasionally the first inflammatory symptoms are intense, but the acuity, visual fields and optic papilla may remain normal for a long time in spite of iridoplegia and discoloration of the iris. These are the cases in which the actual beginning of the disease is not sharply defined from the prodromal period. In these cases iridectomy can effect a complete recovery many months after the outbreak. Even though the visual field and optic papilla are normal during the remissions, central vision may be considerably reduced. The cure seems to be just as permanent here as in the initial period. In malignant cases, as early as a few weeks after the first attack, conditions may be much more unfavorable for operating; in fact, there are fulminating cases in which vision is destroyed forever, so that after the first few weeks nothing is of avail.

2. The prognosis is different as soon as the visual field is constricted. A moderate concentric contraction is the most favorable. It occurs far less frequently, however, than a marked constriction coming in from one side; that latter affects the prognosis the more it approaches the midline. The condition of the papilla is equally important. When the papilla is but little cupped and, on the other hand, the field is decidedly cut down, there is naturally only slight improvement. This is particularly true of the visual acuity but also applies to changes in the field which occasionally may increase four-fold. The improvement usually continues. If, on the other hand, well marked cupping is associated with a high degree of contraction of the field, which is unfortunately the most frequent condition, a warning against too hasty an optimism is hardly necessary.

3. Tension of the globe, iridoplegia, corneal anesthesia and shallowing of the anterior chamber are favorable in that they prove the reduction in vision to be attributed partly to increased pressure, on which iridectomy has a beneficial action. This is also true of clouding of the aqueous and vitreous.

4. If the improvement in an advanced case of glaucoma is not permanent

following iridectomy, the decrease in vision is not accompanied by symptoms of a fresh glaucomatous choroiditis. One should not speak, therefore, of a recrudescence of the original disease; the blindness must be caused by a continuation of the disease in the optic nerve. In a few cases which are exceptional, the subsequent deterioration occurs with symptoms of a rise of pressure.

5. In all cases of glaucomatous blindness an iridectomy has the advantage of alleviating the existing inflammation and the ciliary pain. The ophthalmologist who knows the torture which these blind eyes cause patients for years will greet the effect of iridectomy most heartily. Treatment with frequent blood-letting and narcotics is not necessary any longer.

Iridectomy and Chronic Glaucoma

Although it was on patients with chronic glaucoma that I first performed iridectomy, I yet cannot pass final judgment on this method of treatment in this group. Since the therapeutic value of the operation in any case exceeds that of all other remedies that have been tried, it is clearly necessary to continue to multiply the observations.

In general, a rather early cupping is unfavorable; hence, an extremely early diagnosis is of essential importance. This is not made as easily as in acute glaucoma, in which at the first inflammatory attack an iridoplegia can be discerned easily. Once cupping of the optic nerve occurs, it never disappears.

Iridectomy in Amaurosis with Cupping of the Optic Nerve

I have never observed any direct curative value of iridectomy in these cases. I have never seen improvement of visual acuity or widening of the visual fields beyond the limits of error in observation.

Concerning the operative procedure itself, I have little to say. A piece of iris is excised as in operations in which an artificial pupil is formed. The following points should be observed:

1. The wound must be as eccentric as possible so that the point of entrance is about one-half a line out in the sclera and the internal wound just at the limbus. In this way it is possible to draw out the iris up to the point of its ciliary insertion; this seems to be necessary for a good result. Any deviation of the internal wound from the limbus will diminish the size of the coloboma considerably.

2. Since the excised piece must be as large as possible, a broad, lance-shaped knife should be used, or the usual knife must be thrust in rather deeply. The operation differs, therefore, from that for the formation of an artificial pupil, in which one should excise only a medium-sized piece of iris for optical reasons. The more severe the symptoms and the higher the tension, the more iris would I advise being excised. There is little choice as to the site of the operation. I usually make my incision toward the nasal side; if the cosmetic effect is considered on account of the age of the patient, the incision can be made above this area, although I find that the colobomas made to the nasal side are scarcely noticeable in dark eyes. The excision above is rather difficult and demands a

greater rotation of the globe with the ophthalmostat, perhaps producing a greater inflammation.

3. The aqueous must be evacuated carefully, because too sudden a release of the pressure may cause numerous hemorrhages. In glaucoma, however, these massive hemorrhages tend to occur less frequently than in cases of iridochoroiditis with atrophy of the globe, probably because of the relatively greater pressure after the escape of the aqueous. On the other hand, from the very nature of the disease there is a disposition to rupture the blood vessels. Whether this is due to direct involvement of the wall of the vessel or to venous stasis, I cannot say. I have noted the presence of retinal hemorrhages many times. During the outflow of aqueous I usually exert slight pressure with the finger on the globe. A compression bandage is put on immediately after the operation, and loosened a few hours later. I have not found any other after-treatment necessary. Even when the operation is undertaken at the peak of the inflammation, the symptoms subside spontaneously. It may be necessary in exceptional conditions to apply some antiphlogistic remedy in order to hasten the subsidence of the inflammation. Naturally in these cases the eyes must be more protected from the light and the usual precautions more strictly observed than in the ordinary operation for an artificial pupil.

If the statements concerning the action of iridectomy are summed up, the following facts appear:

1. The surest results are obtained in those cases in which one eye is threatened after the other has become blind. In such cases it is the duty of the physician to refer the patient as soon as possible to an oculist for strict observation, and, vice versa, it is the duty of the oculist to warn the family physician to look for those symptoms which call for operative intervention.

2. Once the glaucomatous process has set in, the results are the more favorable and permanent the earlier the operation is performed. In the acute cases in which vision is lost almost immediately, iridectomy must be performed whenever possible in the first few days of the disease. This is of the utmost importance. Previously a glaucomatous eye was considered incurable the moment the diagnosis was made. It was comparatively unimportant, therefore, which type of medical treatment was used and whether this was instituted relatively early or late. A physician never had to reproach himself for delay in this respect. If I am not mistaken, conditions now are changed. An eye which has been blinded from acute glaucoma may as well excite suspicion of neglect as a badly set fracture, or atresia pupillae following simple iritis.

3. It has been shown that iridectomy is not suitable for all stages of the disease but that its action in a later stage, at least in some cases, is extremely uncertain. It is sad to see the number of incurably blind persons who make long journeys because they think their disease is still curable.

I adopted this treatment with the idea of diminishing the intraocular pressure. Pursuit of this point of view seems to have obtained a result. At the same time, this is not a proof of the correctness of the explanation. It is possible that the effect of iridectomy is extremely complex. A decrease in the secreting surface

of the iris might account for a reduction in the quantity of the fluid, but as yet information is lacking as to how much less aqueous is secreted in these cases and whether such a deficiency could explain such a striking change in intraocular pressure. The cooperative effect of the muscles of the iris with the tensor choroidea, which was pointed out in a recent theory of accommodation, might explain how the excision of a piece of iris would produce a diminution of intraocular pressure by a relaxation of this muscle. The persistence of accommodation after the coloboma has been made, however, does not support this view. Perhaps interference with the iris acts primarily on the choroidal circulation, the therapeutic pressure-reducing effect being only secondary. The presence of the hemorrhages proves that iridectomy in glaucoma is of considerable influence on the ocular circulation. The treatment, undoubtedly, will be still more efficacious when ophthalmologists are able to analyze more correctly all the foregoing points. It is conceivable that in selected cases the ordinary excision is not sufficient, but that removal of large pieces of iris will make the operation more successful. As already stated, the pieces of iris should be larger in proportion as the case is more severe.

The whole subject of glaucoma is open to the most varied investigations. After the marked change in our views on glaucoma produced by the first ophthalmoscopic examinations, I felt that further investigation was imperative. The difficulties which I encountered are apparent to any unprejudiced reader. I hope that I have assisted in solving some of these and that some one who is better equipped than I will soon bring this difficult task to a more happy conclusion.

Comment: Glaucoma was an incurable affection until von Graefe demonstrated the value of iridectomy. Acute glaucoma was originally confused with iritis. In 1813 Beer first recognized that certain cases, which he called arthritic iritis, had special characteristics; and in 1829 Sir William Lawrence identified the arthritic iritis of Beer as acute glaucoma, but the treatment of the new entity continued to be the same as that for iritis. The deleterious action of mydriatics, likewise discovered by von Graefe, was not noted till 1868. This observation led Laqueur to the thought that miotics should be beneficial and the consequent use of eserine, the first medical treatment of glaucoma of any value. Von Graefe attributed the curative effect of iridectomy to the reduction of the secreting surface of the iris, but this theory was discarded when the ciliary body was proved to be practically the sole source of intraocular fluid. The tension of the normal eye is not diminished by iridectomy. Not till 1876 was faulty excretion implicated; in that year Adolph Weber and Max Knies independently noted adhesions of the iris base to the cornea in eyes enucleated after congestive glaucoma. The validity of this view has been recently confirmed by tonography. In 1938 Otto Barkan proposed the separation of the primary glaucomas of the adult into two entities designated as narrow angle (or angle closure) and open-angle (or trabecular). The mydriatic provocative tests give a positive result in narrow-angle glaucoma only. Doubtful cases of open-angle glaucoma are best diagnosed by combining tonography with the water-drinking test. If iridectomy is performed early enough in narrow-angle glaucoma, the filtration angle is permanently opened and the disease is actually cured. As the results of iridectomy in chronic glaucoma were frequently disappointing, De Wecker in 1867 proposed an operation to produce a filtering cicatrix. As the idea became accepted various procedures for this purpose were

developed in rapid succession: cyclodialysis by Heine in 1905, iridosclerotomy by Lagrange in 1906, iridencleisis by Holth in 1907, and corneo-scleral trephination by Elliot in 1909.

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BIOGRAPHICAL NOTE

Albrecht von Graefe (1828–1870) was born in Berlin and graduated in medicine from the University of Berlin in 1847. He then visited Prague, where he was influenced by Arlt to specialize in ophthalmology. He continued postgraduate study in Paris under Sichel and Desmarres; in Vienna, under the Jaegers; and in London, under Critchett and Bowman. Both his father and his uncle had done work in ophthalmology and contributed original observations. His cousin and one-time associate, Alfred Graefe, two years his junior, became a celebrated ophthalmologist, co-editor of the Graefe-Saemisch Handbuch der gesamten Augenheilkunde, and was memorialized by the founding of the Graefe medal. Donders, while visiting the historically first World Fair, that in London in 1851, met Bowman and von Graefe; and forthwith the trio inaugurated a lifelong friendship. Von Graefe had started a successful practice in Berlin the year previously. He was one of the first to fully appreciate the newly invented ophthalmoscope, exclaiming: "Helmholtz has uns eine neue Welt erschlossen!" Von Graefe confirmed the discovery of the cupped disk in glaucoma by his favorite student, Adolph Weber (1855); described the ophthalmoscopic pictures of embolism of the central retinal artery (1859) and of choked disk (1860). In 1854 von Graefe established single-handedly the Archiv für Ophthalmologie, now the second oldest eye journal in continuous circulation, the oldest being the Annales d' Oculistique, founded in 1838. The first volume of von Graefe's Archiv contained 481 pages of which 384 pages were contributed by himself with discussions of keratoconus, ocular muscles, diphtheritic conjunctivitis and the arterial pulsation in glaucoma. In 1856, von Graefe introduced clinical perimetry and stressed the importance of visual fields in diagnosis, and in 1857 he announced the cure of acute glaucoma by iridectomy. He also noted the lid-lag in exophthalmic goiter (1861), modified the cataract operation (1865), improved the operations for strabismus, made notable observations on sympathetic ophthalmia and reported the secondary glaucoma induced by rapid swelling of the crystalline lens (1869). His life was one of unhesitating sacrifice of self to ophthalmology, to teaching and to his patients in spite of continuous feeble health. In 1858 his recurrent hemoptysis and pleurisy became severe, and in 1870 he died of tuberculosis at age 42. How true that "we live in deeds, not hours"!

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Reports from Abroad

BELGIUM

In a previous paper in this journal (1956, *1*, 194) a survey was given of the scientific activities at the Ophthalmologic Clinic of the University of Ghent (Professor J. François). This paper presents a survey of the investigations made in other Belgian university clinics.

1) At the Ophthalmologic Clinic of the University of Brussels (Professor Léon Coppez) Dr. Zanen is making important investigations into acquired central dyschromatopsia, with the aid of a personally designed instrument. Dr. Pierre Danis is investigating electroretinographic changes produced in rats by intra-arterial injection of potassium, veratin and narcotic drugs. Dr. Brihaye is studying the vascularization of the optic nerve by microinjection of anatomic specimens, while Dr. De Laet is concerned with the tension in the central retinal artery and its changes in pre-eclamptic conditions. Professor Léon Coppez, who in 1956 presented the Belgian Ophthalmological Society with an excellent report on the clinical aspects of concomitant strabismus, continues his investigations concerning his operation for detachment of the retina, done with the aid of a thermometric electrode and by a technique of his own design.

2) At the Ophthalmologic Clinic of the University of Louvain (Professor M. Appelmans) investigations are being made into blood coagulation factors in the aqueous humor (Dr. J. Michiels); electron-microscopic investigations are made into the vitreous body and the ocular membranes (Dr. L. Missotten), and into the distribution of radioactive phosphorus in animal organisms and changes in the structure of the eyeball (Dr. Wouters).

3) At the Ophthalmologic Clinic of the University of Liège (Professor R. Weekers) current investigations have two main objects, *viz.*: the early diagnosis of glaucoma and the etiology of concomitant strabismus. *a*. The early diagnosis of glaucoma requires exact determination of intraocular tension. A gauging and standardizing station for tonometers has been established.

Professor Weekers and his co-workers are attempting to introduce, in clinical routine, determination of ocular rigidity, using Goldmann's aplanatic tonometer. Their object is to enhance the exactness of determination of the facility of outflow by clinical and experimental investigations. On the other hand they are investigating visual functions by very sensitive methods, *viz.*: quantitative perimetry, skiascotometry, determination of the critical flicker fusion rate, investigation of dark adaptation of exact localized regions in the visual field, etc.

b. The study of the etiology of concomitant strabismus, based chiefly on examination of twins, has shown that ametropia is hereditary whereas strabismus, amblyopia and absence of binocular vision are not; the latter are merely occasional complications of ametropia. These investigations, and other findings demonstrating the importance of sensory factors, have convinced Professor Weekers of the necessity to correct ametropia in early childhood and to operate

as soon as possible in cases of strabismus which fail to respond completely to the wearing of correcting glasses. The functional results are encouraging both as to prevention of amblyopia and in restoration of binocular functions.

Another manifestation of the scientific activity in Belgium is found in the Belgian Ophthalmological Society, which meets three times a year. Two sessions are dedicated to miscellaneous communications and one session is reserved for the discussion of a report. The last reports were on the following subjects: sulfonamides and penicillin in ophthalmology (A. De Jaeger and R. Weekers), gonioscopy (J. François), anatomy, physiology, pharmacology and semeiology of the pupil (A. Hoorens, C. Heymans, L. Coppez and J. Coppez), congenital glaucoma (J. Kluyskens), exophthalmos of endocrine origin (P. Danis and J. Mahaux), antibiotics (J. Michiels), acquired central retinal dyschromatopsia (J. Zanen), allergy in ophthalmology (A. Potvin and A. Bossu), the surgical treatment of paralytic strabismus (R. Weekers and P. Daenen), clinical aspects of concomitant strabismus (L. Coppez) and ocular complications in diabetes (L. Alaerts and J. Slosse).

Subsequent reports are to deal with heredity in ophthalmology (J. François), the early diagnosis of glaucoma (R. Weekers *et al.*) and ocular manifestations in dermatoses (Lebas).

PROFESSOR J. FRANÇOIS
Ghent, Belgium

Ophthalmic Meetings

PAN-AMERICAN INTERIM MEETING

This is the report of the Pan-American Interim Meeting which was held in New York April 7th to 11th. Readers need not be reminded that New York is a wonderful place to have a meeting, and this, coupled with a good program, brought an unusually large attendance.

The papers were excellent and the two symposia, one on fundus diseases and the other on surgery, were outstanding. In the latter, Paul Chandler made an interesting point in discussing the choice of operation in glaucoma cases in which tension had been high for some time and which therefore had possibly developed peripheral anterior synechiae. As is well known, if such synechiae have developed, a filtering operation is the procedure of choice; it they have not, a peripheral iridectomy should be done. The problem is whether or not such synechiae are present. Dr. Chandler suggested making an oblique corneal incision with a Wheeler knife, evacuating the chamber and then re-injecting saline into the chamber. He said this results in a definite deepening of the chamber so that gonioscopy done right on the operating table now permits a view of the angle. It is then easy with the gonioscope to decide whether P.A.S. have formed and, if so, to what extent, and then to proceed immediately with either the iridectomy or the iridencleisis on the basis of this information.

In this same symposium, Dr. Norton of New York emphasized the importance of using the Schepens indirect ophthalmoscope in retinal detachments both preoperatively and at the time of surgery. He felt that a scleral depression in conjunction with the ophthalmoscope was most important, but said that it took six months of constant practice to master the technique.

Dr. Dohrmann Pischel gave an excellent talk in which he discussed some of the operative complications frequently encountered. He emphasized the importance of proper localization of retinal breaks and said that, ideally, the scleral buckle in a lamellar resection should be located in such a way that the tears are on the crest or anterior to the buckle. He said that the surgeon should not hesitate to detach as many muscles, including the obliques, as necessary. If for technical reasons, it is impossible to locate the resection in the ideal way, then one should make it anteriorly, and diathermize the areas of the tear. He prefers to make perforating diathermy punctures back of the area of the resection to insure adequate drainage of sub-retinal fluid.

He made several excellent suggestions in regard to drainage of sub-retinal fluid. If there is a relatively flat detachment and the surgeon is in doubt about how much sub-retinal fluid he will be able to drain, he should make his scleral resection about half as long as he considers optimal. If this short resection can be easily closed, then, with only slightly more technical difficulty, he can proceed to lengthen the resection.

He mentioned several tricks in case drainage of sub-retinal fluid is not adequate through the perforating diathermy openings. One can use suction with an eyedropper or, if this does not work, one can dilate the opening with a punctum dilator. If this still does not work, he suggested making either a trephine opening or a scratch incision down to the choroid and perforating it with a Ziegler knife to a depth of only 2 or 3 mm. Angling the knife one way or another may succeed if introducing it straight does not produce results.

Dr. John Dunnington in discussing cataract surgery stressed the importance of preoperative preparation. He expressed a good deal of skepticism in regard to the insertion of various lenticuli but said that, in Europe at present, the trend is toward the use of implants into the anterior chamber.

Dr. Townley Paton and Dr. Castroviejo talked about the broadening indications for corneal transplants. Dr. Paton said that often times a second or even third graft might remain clear when a first became cloudy.

There were many fine individual papers and movies. Dr. Pico's paper on retinal detachment was particularly good.

Dr. B. J. Curtin presented an interesting paper on aneisikonia following retinal detachment surgery in which he showed that the image in the operated eye in a number of cases was smaller than in the normal eye. This difference amounted to five per cent in a number of cases and as high as eight per cent in one case. Dr. Arthur Linksz, who discussed the paper, postulated that there might be stretching of the retina from tension which would have the effect of spreading the percipient elements more widely with a resultant smaller image.

This was probably the most original and important of the papers and certainly bears further investigation.

One of the highlights of the meeting was the banquet. Ambassador Adolph Berle gave a fine talk on the importance of physicians in creating a better world atmosphere and Dr. Howard Rusk gave an inspiring talk on the effect that help in rehabilitation could achieve in our relationships with men of other countries.

It was a most successful and pleasant meeting.

DANIEL SNYDACKER

CONGRESS OF THE OPHTHALMOLOGICAL SOCIETY OF INDIA

The Congress of the Ophthalmological Society of India was held at Bangalore from February 21 to 25, 1957.

The Adenwalla oration, given every alternate year, was given by Dr. S. N. Cooper of Bombay, who placed before the assembly an illuminating account of antigenic properties of lens proteins. He emphasized the importance of the subject and demonstrated specific antibodies by precipitin tests. It is his opinion that lens proteins are the most antigenic. He also stressed the importance of treatment by very small doses of lens proteins, although he admits that many setbacks have occurred in his cases. A hope has been offered that by judging the intensity of precipitins in the aqueous humour it may be possible to strike an optimum dose of lens protein which should be administered. Two interesting

findings reported by him are of some value. First, fish lens proteins have no antigenic properties. This is perhaps not yet acceptable in view of many mishaps that have been reported in the past by an attempt to desensitize patients by fish lens proteins. Second, probably cysteine has no antigenic role as against the views of Agarwal. He is not unequivocal in this contention.

A symposium on trachoma was held. The four papers which deserve special mention are:

(1) A mass survey conducted by Dr. Radonovich under the auspices of World Health Organization, from which he suggested that even in India there is a great disparity in the incidence of trachoma, the sandy and cultivable area being the worst sufferer. He also suggested that greater recognition should be given to other methods of spread than mere contagion. It is probably linked with the personal hygiene of the people. The facts are well recognized in the country but they have for the first time been scientifically stated.

(2) The virus culture of trachoma was done by Prof. Srinivasan. He could successfully transplant the cultured virus in human volunteers. The paper is interesting from the point of view of its novelty in India.

(3) Cytopathology in trachoma was presented by Agarwal. He was the first to state that trachoma has a definite cytological pattern and laid down five criteria of diagnosis namely, (a) degeneration of epithelial cells, (b) presence of inclusion bodies, (c) multinucleate epithelial cells, (d) germinal center cells, and (e) laber cells. The same was reported by Thygeson a few months later and this paper confirmed the findings. In addition, the paper included the cytopathologic findings in xerosis and phlyctenular conjunctivitis which covered the material already published by Agarwal in Ophthalmologica.

(4) The fourth interesting item was the panel discussion on therapy of trachoma. Among those who participated in the discussion were Prof. Tulsi Das, Dr. Radonovich, Prof. Larumande (Algiers), Dr. Srinivasan (representing the old guard), Prof. K. N. Mathur and Prof. Agarwal. The discussion was convened by Dr. Y. K. C. Pandit. There was a wide divergence of opinion on whether the antibiotics and sulphonamides had any effect on the trachoma virus. It was agreed that copper has still a place in the treatment, especially in pannus without ulceration. The discussion suggested that there is hardly any choice between the various antibiotics. In a later paper, "The Modern Therapy of Trachoma," Agarwal made an appeal for the trial of bile salts (30 per cent) applied in the everted lids because of its epitheliolytic properties. It was agreed that sulphonamides probably offer the best line of treatment so far available. Under the pilot trachoma project various drugs will be tried and a clearer picture is likely to emerge at the end of this study.

Another interesting article was the biomicroscopic study of the conjunctival vessels by Prof. K. N. Mathur. The work is being done under the auspices of Indian Council of Medical Research. He feels that conjunctival vessel examination reveals hypertensive changes earlier than increase in brachial pressure. The findings are not yet conclusive but give promise for the future.

LALIT P. AGARWAL

Book Reviews

An Atlas of Diseases of the Eye, by E. S. Perkins and Peter Hansell. *(Little, Brown and Co., Boston, 1956, 85 pp., 201 figures, $10.00) is a series of colored illustrations of a variety of diseases of the eye. It is reviewed here by P. Robb McDonald, a contributing editor to The Survey of Ophthalmology.*

This little book of less than one hundred pages contains more information than many books many times its size. Fortunately, the cost of publication was almost entirely underwritten by Roche Products Ltd., so the price is not prohibitive. The value of the book lies in the superlative illustrations and photographs of the common external diseases and the fundus drawings. Most of the reproductions are in color and the accompanying clinical descriptions, which also include a few sentences on the pathologic changes, are evidence of a most careful revision. The sections on the fundus in systemic and local disease are exceptionally well done. The reproductions are beautiful and the accompanying descriptions succinct.

This book will prove invaluable in any hospital library and should be on the shelf of all diagnosticians. Most ophthalmologists will want it for teaching purposes, even if they do not learn anything new from its perusal. The advanced student in ophthalmology will not learn anything new but will have at hand a ready reference to most of the conditions seen in the general practice of ophthalmology. This volume is a credit to the editors, the publishers, modern photography and the generosity of the sponsors.

Augensymptome bei Hirntumoren (Ocular Symptoms in Tumors of the Brain) by Alfred Huber is Vol. VII in Sammlung Innere Medizin und ihre Grenzgebiete, edited by P. H. Rossier and O. Spuhler. *(Hans Huber, Publisher, Bern and Stuttgart, 1956; 404 pp., 192 figures; Linenbound, 56 Swiss francs.) It is reviewed here by Arthur Linksz, contributing editor to the Survey of Ophthalmology.*

"Ocular Symptoms in Tumors of the Brain" by Alfred Huber is based on personal experiences gathered in the neurosurgical clinic of the University of Zurich from some 1600 cases. It is not a book written by a neurologist or neurosurgeon on symptomatology, handling, therapy, results or statistics in brain tumors. To the ophthalmologist, acting as consultant, it gives some basic information on the nonocular signs and symptoms of brain tumors, as much of it as is certainly necessary if he wants to partake in discussion intelligently. To both the neurologist and the ophthalmologist it gives an excellent, manysided, concise and still sufficiently complete description of the ocular signs and symptoms of tumors of the brain, of the methods and techniques used in detecting, evaluating and differentiating these signs and symptoms.

The first chapter of the book deals with the methods of neuro-ophthalmologic examination, first with subjective symptomatology, then with objective ex-

amination. It is amazing how much about ocular involvement can be learned from a good anamnesis and examination including field defects, disturbances of simpler and higher visual functions, alexia, agraphia, diplopia, pain, photophobia, etc. The objective examination of the patient suspected to have a brain tumor encompasses, of course, almost all of ophthalmodiagnostic methodology, since the examination of the lids, the lid tissue, the cornea, the pupil, the mobility and, last but not least, of the eyeground all will or can contribute to the proper diagnosis. That visual acuity, even color vision and dark adaptation, be not forgotten hardly needs mentioning. A thorough discussion is reserved to the study of the peripheral and central field and the differential diagnosis of nystagmus. The American reader will be pleased to see that the Lancaster red-green test for the diagnosis of motor disturbances has found its way into the Zurich neurosurgical clinic. On the other hand, he will learn about the type quantitative perimetry which became possible by the use of the Goldmann perimeter and about the Amosler central vision tester—both Swiss contributions to this important phase of the ophthalmodiagnostic process not yet widely enough known or applied in the United States. For the study with the Bjerrum screen the author prefers the 2 meter distance (and even the 6 meter recommended by Vogt).

Whatever the merit, however, of these sections of a book on the ophthalmodiagnostic process in tumors of the brain its value as a contribution stands or falls with the particular handling of the problem of papilledema. The author was certainly aware of the significance of this problem and the best part of a chapter is devoted to it. Especially interesting is his discussion of the early signs of papilledema. The publisher would have added immensely to the value of the book had he replaced the small black and white fundus photographs with colored photographs (or even drawings) of sufficient format. It was an excellent idea to include a discussion of the differential diagnosis of papilledema and a description of conditions like papillary edema in malignant hypertension, papillitis, pseudoneuritis and colloidal degeneration ("drusen").

The body of the book, following these two introductory chapters, deals with the local symptomatology of brain tumors. The contents of these chapters cannot be indicated even in outline. Intrasellar, suprasellar and parasellar tumors are discussed at due length. The visual fields are very instructive, especially in those cases where Goldmann and Bjerrum fields of the same case are shown next to each other. Here are some good roentgenograms and photographs of patients and of specimens. On the other hand the surgical sketches, pre- and postoperative, are—at least to one reader—rather pointless, even meaningless.

A chapter on pseudo-tumors, including subdural hematomas, brain abscesses and aneurysms concludes this valuable book and there is a good index and a magnificent bibliography. Translation into English should turn out to be a successful publisher's venture.

Clinical Practice

ACCOMMODATION AND REFRACTION

SIDELIGHTS ON REFRACTION

F. A. Williamson-Noble

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Several observers have found night myopia in amounts varying from 0.5 D to 0.2 D. It would appear that the myopia is due to accommodative changes in the lens and not to dilatation of the pupil exposing more of the lens periphery and allowing of greater spherical aberration, since artificial dilatation of the pupil by homatropine reduces the change in focus from the usual 1.0 D to 0.1 D. The rate of development of the myopia on entering a dark room seems to parallel that of dark adaptation. One observer suggests that in conditions of low illumination, an individual would expect to be able to see things only if they were fairly close to him. In consequence there is a slow gradual increase in the tonus of the ciliary muscle sufficient to alter the refraction of the dye by a diopter or so.

Another ingenious theory is that, as the pupil dilates, there is a gradual slight foreward displacement of the lens, producing some myopia. Chromatic aberration has also been invoked, the light adapted eye tending to use the yellow-green part of the spectrum and the dark adapted, the green. However, this would only account for about 0.38 D of myopia.

The increase in curvature of the anterior surface of the lens in the dark adapted eye was measured in 1953 and found to account for only 0.8 D. These observers suggested that peripheral spherical aberration must contribute in making up the difference.

Another observation noted is the phenomenon of space myopia. Subjects gazing into an empty but bright field involuntarily produce an average of 0.50 D of accommodation.

The author briefly discusses the phenomenon of the "bifocal eye"; that is, an individual in the presbyopic age group who has good near vision while wearing only a distance correction. Actual differences in refractive errors due to corneal or lens changes in the various meridians of the pupil as measured by Fincham's coincidence refractometer may account for this. Occasionally an extremely miotic pupil may accomplish the same thing.

The author describes his experiences with a bifocal contact lens. Putting the add in a central position was unsuccessful because of blurry distant vision when the pupil is miotic. The segment could not be elevated since the tear film rendered

it ineffective. Segments may be recessed into the front surface of the glass. They may be made of a plug of higher refractive glass fitted into a hole in the lens, or the inner surface of the contact lens may be flattened slightly.

A reasonably successful lens is a scleral type fenestrated contact lens with a lower reading portion and an upper distant portion. The lens follows the eye in horizontal movements, but lags behind in up and down movement. Therefore, on looking down, the lens moves upward relative to the eye, and one looks through the bifocal. A troublesome feature is diplopia when one is not looking through only one segment. This may be eliminated largely by positioning of the head. Image jump may be eliminated by making the optical centers to coincide.

Essential features of an adequate fit on a bifocal contact must include: (1) free motion in a vertical, but not in a horizontal direction over the eyeball; (2) no rotation in the slightest degree; (3) comfort; (4) sufficient air to prevent the formation of Sattler's veil, but not enough to allow a bubble to form in the pupillary area. The technical difficulties of producing such lens is apparent.

Making a bifocal eye by surgical means is postulated. Reference is made to the technique of scarification of the inner surface of the cornea to obtain changes in refraction.

An instrument for subjective estimation of refractive errors has been devised. An emmetropic eye looking through two pinholes close together at a point source of light will see one light. A myope will see two lights, the right one from the left hole; but a hyperope will have a "homonymous diplopia." This instrument has two bar-shaped movable light sources. Therefore, a patient with a refractive error will see two pairs of lights through the 100 pinholes. He can align the left bar of one pair with the right bar of the other and the approximate refractive error for that meridian may be read from a calibrated scale based on the amount one light had to be moved in relation to the other. This may be repeated in various meridians.

Comment: Nocturnal myopia has been the subject of a number of papers since the first observations in 1941, and there seems now little doubt as to its occurrence. It has been suggested that is is a form of psychic proximal accommodation, that it is due to chromatic aberration in the eye, that it is caused by changes in pupillary size, or that it is due to an actual increase in the tonus of the ciliary muscle. The latter now seems to be the more generally accepted theory.

The influence of pupillary size apparently has not been entirely ruled out by those who have experimented with the problem. Experimental dilatation of the pupil by homatropine does not produce night myopia, but then it must be remembered that homatropine is also a cycloplegic drug and would tend to produce a diminution in the normal tonus of the ciliary muscle so that it would be quite possible to compensate for increased refractive power in the periphery of the enlarged pupil by a decrease in tonic accommodation. If it could be shown by the use of a rigid control of the entrance pupil by pupillary disks that pupillary dilatation was not involved in the production of the night myopia, we would have to explain the phenomenon largely upon the basis of accommodative activity.

It would be well to remember that the normal tonus of the ciliary muscle produces a constant, though perhaps slightly variable amount of accommodation, which is greater during youthful life and which diminishes with age, not as the result of any great change in muscular tension, but because of the gradually increasing sclerosis of the crystalline lens.

As far as we know at present, there are four possible stimuli sources which produce accommodative responses. They are: (1) the normal tonus of the ciliary muscle which produces what may be called "tonic accommodation," (2) the blur produced by imperfect retinal images which reflexedly produces that which may be called "retinal accommodation," (3) accommodation produced by an association reflex from convergence, "convergence accommodation," and (4) accommodation produced by the proximity of the object observed, which may be termed "proximal accommodation."

It can be seen that of these four, only the convergent accommodation could be ruled out as implicated in the production of nocturnal myopia if it is found to be upon an accommodative basis. Tonic accommodative changes are possible, retinal accommodation may be stimulated by the difficulty in seeing resulting from low illumination, and proximal accommodation, as suggested by one of the previous investigators, is possible, although less likely.

"Bifocal eyes" are defined by the author as those possessed by elderly persons who apparently have an abnormally great amplitude of accommodation. This is not an unusual phenomenon in a large refraction practice, but it almost invariably is associated with early pathologic changes in the crystalline lens, including some liquefaction of the cortex, and is therefore a type of early cataract change. This phenomenon is one proof of the innervational basis of accommodative activity.

Presbyopia, in this view, involves little change in the tonus and contractility of the ciliary muscle during active life, the loss of accommodative amplitude being due almost entirely to a lessening response of the crystalline lens to normal innervation because of its increased sclerosis. Thus, many elderly individuals who present liquefaction of the cortex as an early development in cataract may regain a considerable amount of accommodative amplitude and be able to again read without bifocals. As a rule, however, there is some reduction of visual acuity both for distance and near because of the lens changes.

Pupillary size is, of course, another factor to be considered. If the crystalline lens is clear enough and the pupil small enough, depth of focus may compensate largely for lack of accommodative ability, and this should be kept in mind in elderly individuals who have very small pupils and clear lenses. In fact, one of the popular "eye exercise and throw away your glasses" programs is based primarily upon the obtaining of small pupils by exposure to high illuminations, such as gazing at the sun and occluding the eye momentarily and repeatedly by "palming."

The third refraction sidelight presented by the author has to do with bifocal contact lenses, a project which illustrates very well the curious objection to the wearing of glasses which is very marked on the Continent, although somewhat less so in the British Isles. As the author has found out in his various experiments, the only possible way to have any success with bifocal contact lenses is to have one which will move vertically as the patient looks up and down. This, to say the least, is not very good contact lens practice however successful it may be as an expedient in permitting the use of a contact lens with two focal areas. In view of the requirements for the successful prescription and fitting of contact lenses which would permit movement in a vertical direction only, it is not likely that ophthalmologists in the United States will spend much time experimenting with them.

Scheiner's experiment, which dates back to the year 1619, is suggested as a basis for a

subjective refraction procedure by Fabre of Lille. This, again, would be of little interest to American ophthalmologists because of the relatively great error which past clinical experience has shown to be inseparable from procedures based upon this principle. American ophthalmologists, with their insistence upon accuracy in the diagnosis and correction of refractive errors, are not likely to be content with the approximate values which would be obtained by this procedure. It is interesting only in that it again demonstrates the validity of Scheiner's observations and of the principles of optics upon which they are based.

EDWIN FORBES TAIT

CONJUNCTIVA AND CORNEA

NOTES ON CORNEAL GRAFT SURGERY

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J. Maine M. A., 1957, *48:* 1–4

The transplantation of a portion of the cornea, a total penetrating graft or a subtotal lamellar nonpenetrating graft, is a sound surgical procedure with technical requirements which are no more difficult than those connected with a cataract operation or with certain types of glaucoma surgery. The cases in which penetrating corneal surgery may be considered suitable are those in which there is a scar that invades the corneal stroma to the level of Descemet's membrane. Lamellar keratoplasty is indicated in cases in which clouded cornea overlies normal cornea above Descemet's membrane. Lamellar keratoplasty is often needed as a preliminary procedure, to be followed by a penetrating graft after the patient has recovered from the first operation. Corneal grafting should not be carried out as an elective procedure until any inflammation that may have been present has become quiet. This applies especially to patients with postinflammatory conditions with posterior synechiae, such as lime burns; in those with corneal opacities due to ulcerative keratitis; and in those who have sustained impact and penetrating injuries, as in mine accidents. Cataract extraction, if needed, should be performed after a successful corneal grafting.

A second graft operation is not infrequently necessary, because, although the first graft may take successfully, it often becomes opaque. Corneal graft opacification is seen especially in certain corneal conditions, including those caused by trauma, and in cases with pannus, symblepharon, and corneal vascularization. In 1932, Castroviejo showed clinically, on the basis of observations in more than 300 partial penetrating keratoplasties, that opacification of the graft fol-

lowed technical defects and complications such as poor coaptation of the graft to the recipient corneal margins, infection, and incarceration of corneal tissue, presumably iris and lens capsule, as well as vitreous.

The ideal indications for corneal graft surgery are found in keratoconus, quiescent interstitial keratitis, and cases of corneal scarring—old, healed, and quiescent—resulting from ulcerative keratitis. Therapeutic grafting because of actual or impending corneal perforation, as with a descemetocele, is a logical procedure for saving the eye, but not for securing the final correction or the best improvement in visual acuity. These must usually be attended to after further graft surgery.

Special care must be used in preparing the graft recipient area in eyes with traumatic perforation. Sufficient marking of the cornea around the graft site with a sharp trephine stained with dye and an especially careful removal of the corneal section are essential. A perfect pair of corneal scissors should be used in the removal, because the condition of the recipient eye may not permit the cutting trephine to be used as extensively as might be desired. The graft sutures, because of possible inaccuracy in the incision line, must be interrupted; they should be placed very carefully. Each suture, as it is tied, is to be followed by the next suture at a position exactly opposite on the edge of the graft. This permits adjustment of the graft to the graft site. More sutures are needed than usual, because the purpose of the graft is not so much to conserve visual acuity at the outset as it is to save the globe.

The major problem in fixation of the graft is the danger of trauma to the graft while attempting to obtain perfect surgical edge-to-edge coaptation with interrupted sutures. Attempts have been made to devise a plan by which overlying sutures could be introduced or some overlying mold or splint could be used to secure this perfect coaptation. Fixation of the graft by means of sutures is still unsatisfactory. Overlying sutures alone are not satisfactory for the fixation of the circular graft. Perhaps the best suturing procedure at present is to use crossing silk sutures and direct approximation 6-0 chromic catgut sutures as an adjunct. Before the present satisfactory catgut-bearing American atraumatic needles became available, the question of suture material presented no problem unless one wished to use catgut as an overlying suture, because there were no needles that could be used with a threaded catgut suture for direct approximation. Clinical experience and some experimental work now suggest the advisability of using catgut for direct approximation. Any suture larger in size than 6-0 chromic suture would be too traumatizing, but whether 6-0 sutures would remain in situ long enough for safe fixation of the graft is questionable.

Undoubtedly, the ideal technique for fixation of the graft would be one in which it would be possible to secure and retain perfect approximation with the least amount of, or better still, no damage to the graft; and in the execution of which it would be possible to use sutures which could be removed if necessary without traumatic complications and to use needles which could penetrate deeply into both the graft and the recipient site without perforation of either. So many difficulties are encountered in cutting a graft with sloping edges that it seems best to cut both graft and recipient site with vertical edges.

The most significant immediate postoperative complications are dislocation of the graft; loss of the anterior chamber; anterior synechiae; delayed healing in aphakia from the interposition of vitreous fibers between the graft and the recipient cornea; and the most tragic of all, postoperative infection. Some of these complications occur because of the faulty technique and, at least theoretically, ought not to occur. Cases in which the graft is applied therapeutically because of trauma are almost certain to have synechiae, both anterior and posterior; many will have lens damage as the result of the original disease and the trauma of the therapy and the perforation. After recovery from the first graft operation, an effort should be made to correct all complications, except those requiring lens extraction. Finally, a secondary graft should be placed as near the center of the cornea as possible when it is needed for visual acuity correction.

Vascularization of a graft is either the continuation of preoperative vascularization, or especially if deep, a result of premature operation in case the causative disease is still active. Superficial vascularization from the trauma of surgery is not uncommon and is of no great significance because it can be corrected. Vascularization is probably a uveitic response, i.e., the result of the reestablishment or the development of primary uveitis of a type distinct from that caused by tissue sensitization. In these cases, anterior synechiae, which in themselves may be responsible for vascularization, opacification, and a secondary uveitis, are the result, not of a foreign tissue response by the host's ocular tissue, but rather of technical faults in the operation and suturing, or complications of postoperative care, or both.

Special mention must be made of late iris prolapse occurring between the edge of the graft and the edge of the recipient cornea. When this complication, which fortunately is not too common, appears, it should be corrected through a corneal incision at the limbus, at a distance from the site of the prolapse. In this way, the iris can be withdrawn from its prolapsed position through a fresh surgical opening and after the resection has been made with iris scissors and iris forceps, the pillars of the operative coloboma will not be incarcerated in the wound of the original prolapse.

Comment: Most surgeons would agree with Dr. Spaeth that catgut sutures have a limited value at the present time in the fixation of full thickness grafts, particularly in the surgical treatment of conical cornea, where it is desirable to retain fixation for three to four weeks.

In this article, as in previous publications by this author, it is apparent that he is not completely convinced that the late clouding of grafts is due to a donor-recipient sensitivity reaction. The study of Maumenee, and more recently, the experiments in our own laboratory, leave little doubt that this clouding is in fact due to the sensitization of the host by the donor graft. It is time that surgeons interested in keratoplasty accept this as a fact so that they can treat adequately the complication with hormones when it occurs, and in some cases prevent its occurrence by preparatory lamellar grafting.

The author does not describe his method for cutting grafts with vertical edges. In this reviewer's experience, the slope of the graft edge depends on the ocular tension, the pressure and sharpness of the trephine, or upon the use of a rapidly rotating mechanical trephine.

While most surgeons would agree with Spaeth that "cases should not be operated as an elective procedure unless all inflammation has become quiet," it is well to recall some of the writings of Franceschetti who advocates early lamellar grafting in severe herpetic keratitis and chemical burns.

HUGH L. ORMSBY

EPITHELIAL TUMORS OF THE BULBAR CONJUNCTIVA

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Bull. Soc. Belg. d'Ophth., 1956, *113:* 436–464

Epithelial tumors of the bulbar conjunctiva can be divided into two large groups: (1) those resulting from hyperplasia and (2) those resulting from dysplasia. Each of these in turn contains two subgroups, one of which comprises simple epithelial hyperplasia and papillomatous hyperplasia, while the other comprises the intraepithelial epitheliomas and spinocellular or basocellular epitheliomas.

Simple epithelial hyperplasia, which appears as a small whitish plaque or a small gelatinous projection accompanied by increased vascularization, is generally localized at the level of the limbus, on the horizontal meridian, on the nasal side. Like the papilloma, but unlike epitheliomas, this tumor becomes fluorescent under ultraviolet light. Papillomatous hyperplasia, which is found most frequently at the level of the limbus, appears as a small expansive tumor composed of a series of projecting nodular formations centered around a vascular axis, accompanied by congestion that may be quite pronounced. Two varieties of papillomas have been distinguished: (1) the true papilloma, which may be multiple and is usually located near the caruncle or in the superior cul-de-sac, and (2) the malignant papilloma, which is single and which appears near the limbus; even when this tumor is still histologically benign, it is clinically malignant because it tends to progress and to invade the corneal surface.

In the dysplastic group, the intraepithelial epitheliomas appear as flattened, pinkish, lobulated tumors approached from different directions by tortuous turgescent vessels. Each component lobule contains an axial vessel, which comes from within and either makes a hairpin curve before disappearing or spreads out to form several loops or even a small glomerule. Spinocellular or basocellular epitheliomas present this same clinical picture in the beginning but they progress more rapidly, both in extent and in depth.

Clinical and histologic evidence supporting this classification was obtained in 15 patients with epithelial tumors of the bulbar conjunctiva, representing two cases of simple epithelial hyperplasia and three of papillomatous hyperplasia;

four cases of intraepithelial epithelioma and three of spinocellular or basocellular epithelioma; one intermediate between epithelial hyperplasia and intraepithelial epithelioma; one intermediate between papillomatous hyperplasia and epithelioma; and one pseudoepithelioma. The findings in these cases show that further subdivision is unnecessary and confusing. Furthermore, the term epibulbar tumors, which has often been used, is misleading because (1) epibulbar tumors include not only the epithelial tumors but also those that are nevoid, conjunctival, lymphoid, and vascular, and (2) the word epibulbar indicates only the site of the tumor and not its origin; yet the great majority of the tumors referred to as epibulbar have their origin in the bulbar and especially the limbic conjunctiva, invasion of the cornea being a secondary development. Primary tumors of the cornea are, in fact, quite exceptional.

Transitional forms are, of course, common, but the transition from the benign to the malignant usually takes place in stages marked by clinical and histologic changes that fall within one or another of the four groups described. Clinical examination alone is usually not enough for an exact diagnosis and even histologic examination, though indispensable, is not always decisive. Sometimes the the true nature of the tumor can be determined only on the basis of the clinical history, the course of the tumor, and the histologic findings. This was true of the pseudoepithelioma in this series, in which the histologic picture was that of a spinocellular epithelioma, suggesting malignancy. In fact, however, the pseudotumor was a repair process following conjunctival ulceration and it disappeared rapidly under treatment with antibiotics. External irritation and climate may also exert a harmful effect, as shown by the fact that eight of the patients were Negroes; apparently, epithelial tumors of the conjunctiva are much more common in the Belgian Congo than they are in Belgium. In none of these patients, however, had the appearance of the tumor been preceded by a chronic irritation of the eye due to trichiasis, trachoma, leukoma, keratitis, or conjunctivitis.

Epithelial tumors of the bulbar conjunctiva may be treated surgically. Excision is easy and gives good results provided the cut made in removing the pedicle is carried into the healthy tissue. Recurrences, however, have been reported. Diathermic coagulation, with or without surgical exeresis, also gives good results, and treatment with beta rays may be effective if the lesions are very limited. The authors, however, prefer contact radiotherapy, which produces a rapid, complete, and definitive cure. The only complication to be guarded against is cataract, but with a 1 mm. lead localizing apparatus, it is possible to limit exactly the field to be irradiated and to give an adequate dose without injuring the underlying tissues.

Comment: The authors have made an excellent review of the current knowledge of the tumors of the bulbar conjunctiva, and emphasize the fact that the majority have their origin in the limbic conjunctiva, secondarily invading the cornea.

While the reviewer agrees that contact therapy with the low voltage (50 kv) Phillips unit in doses of 5,000 to 6,000 r would result in a cure of most lesions, he feels that even by protecting other areas of the globe with a lead shield, radiation cataract would almost certainly result from such a procedure and dosage. Excision, if deep enough to include

the entire growth, will result in cure in all but the most extensive lesions, and radiation should only be employed in tumor dosage in incompletely removed malignancies. It should be kept in mind that the depth dose of 50 kv rays to the lens is approximately 50 per cent and that the cataractogenic dose of x-rays is approximately 800 r (Cogan).

HUGH L. ORMSBY

DIFFERENTIAL DIAGNOSIS OF SUPERFICIAL FORMS OF KERATITIS AND KERATOCONJUNCTIVITIS

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The formation, two years ago, of a research team for the study of viral keratoconjunctivitis at the University of California School of Medicine gave the authors their first opportunity to analyze cases of superficial keratitis and keratoconjunctivitis on the basis of complete laboratory and clinical examinations. Analyses have now been made in 300 cases according to (1) history and symptomatology; (2) gross and biomicroscopic appearance of the lesions; (3) cytology of scrapings and exudates; (4) bacteriologic and mycologic findings; and (5) virologic and serologic findings. Most of the cases were caused by viruses or unknown agents suspected of being viruses. Excluded from the series were typical cases of bacterial keratoconjunctivitis and corneal ulceration; included were a few atypical cases of catarrhal ulcer secondary to blepharitis or bacterial conjunctivitis in which an immediate diagnosis could not be made. The high percentage of herpetic cases reflects the frequency and importance of this disease in the San Francisco Bay area. A separate report presently to be published will deal fully with herpetic ocular infection as it has been observed in this area during the last 10 years.

The history of the onset and the character of the symptoms are valuable guides to the differential diagnosis and, although their importance is less than that of other parts of the analysis, they are essential to a proper diagnostic survey. In spite of improvements in laboratory techniques, in this series it was still the analysis of the gross and biomicroscopic clinical picture of the disease under study that yielded the most important differential information. The value of this information, however, varied greatly from type to type of keratitis. At one extreme was the keratitis of herpes zoster ophthalmicus, which had to be diagnosed entirely on the morphologic appearance of the combined skin and corneal lesions, with the laboratory still unable to offer useful diagnostic information.

At the other extreme was acute follicular conjunctivitis, which could be identified according to etiologic type only with laboratory aid. Between these two extremes lay the remainder of the cases in which morphology provided etiologic information of greater or less reliability.

Since corneal tissue cannot ordinarily be subjected to biopsy, cytologic study of most of the cases was necessarily limited to examination of exudate smears or epithelial scrapings. Cytologic findings were particularly valuable in identifying vernal catarrh and keratoconjunctivitis sicca, and in differentiating bacterial from viral keratoconjunctivitis. There seems to be every reason to believe that cytologic examination will tend to play an increasingly important part in the differential diagnosis of keratitis and keratoconjunctivitis.

Biopsy of the cornea is not a practical procedure in keratitis, but biopsy of the limbus and conjunctiva can be performed with safety and should be resorted to more often than it is at present. In one case of granulomatous chronic keratoconjunctivitis, a diagnosis of sarcoid keratoconjunctivitis was based on the biopsy findings.

Although viruses have a greater causative importance than bacteria in the nonsuppurative forms of superficial keratitis and keratoconjunctivitis that were chiefly considered in this series, the bacteriologic examination was an essential feature of the diagnostic survey and helped materially, especially in uncovering cases of epithelial keratitis and marginal ulceration due to staphylococci. The distinguishing feature of this survey, however, was the introduction of virologic and serologic methods of diagnosis. These proved to be of special value in the differential diagnosis of herpetic keratitis, acute follicular conjunctivitis, keratoconjunctivitis, and epidemic keratoconjunctivitis. Even in the cases that still resist identification, it seems likely that studies in which more than one type of tissue culture can be employed will, in the future, yield information of etiological value.

Examples of new or recently developed methods used in this study are, first, the serologic diagnosis of epidemic keratoconjunctivitis by the demonstration of a rising titer to APC type 8 virus during convalescence, and the serologic diagnosis of pharyngoconjunctival fever by a similar rise in titer to APC type 3 virus; and, second, the cytologic diagnosis of trachoma by examination of follicular expressions. Improvement in clinical diagnosis is perhaps best exemplified by the fact that it is now possible to divide acute follicular conjunctivitis into six distinct entities. This is a noteworthy advance since 1933, when Morax, in his monograph *Les Conjonctivites folliculaires*, was able to define only two types—inclusion conjunctivitis and acute follicular conjunctivitis, Beal.

The findings in this study, in which the problems of differential diagnosis are considered in detail, serve to emphasize the overwhelming importance of herpes simplex virus as a cause of keratitis and keratoconjunctivitis, and to illustrate the many forms other than the classical dendritic one in which this affection may appear. The importance of diagnosing these atypical forms accurately was brought home by unfortunate reactions to cortisone in certain patients mistakenly given a diagnosis of catarrhal ulcer or phlyctenulosis.

Comment: This careful analysis of a major series of cases shows that most, if not all, cases of keratoconjunctivitis can be classified on an etiologic basis by clinical and laboratory means. While not many practitioners have the opportunity to maintain tissue cultures for virus isolation and typing, much information is to be derived from the ordinary bacterial and cytologic studies made in the ophthalmologist's office. It is perfectly feasible to store liquid culture media indefinitely in screw-capped test tubes, and these are easy to inoculate with a sterile cotton throat swab from the conjunctiva. At the same time, a conjunctival scraping can be taken under pontocaine anesthesia. This can be stained with Wright's stain by the office assistant and examined by the ophthalmologist before treatment is prescribed. A little practice and familiarity with the papers of the California group on cytologic findings will provide many useful clues as to etiology. If time presses, the specimen can be set aside for future staining and study, or carried with the culture tube to the laboratory for reporting by a trained technician. The practice of resorting blindly to empirical treatment not only clouds the picture for consultants but may have adverse effects upon cases of herpetic and fungus keratitis.

HENRY F. ALLEN

SYMPOSIUM: HERPETIC INFECTIONS OF THE OUTER EYE

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Tr. Ophth. Soc. U. Kingdom, 1956, *76:* 187–225

In discussing the virologic aspects of herpetic infections of the outer eye, Dr. Dudgeon stated that herpes simplex is one of the commonest virus infections of human beings. The virus is widely disseminated throughout the population and can be recovered from the saliva of healthy individuals. Two distinct types of infection occur, primary and recurrent. The majority of infants are protected for the first 6 to 8 months by maternal antibody. Primary infection occurs thereafter in children without antibody, most commonly as an asymptomatic infection. Considerable variation is encountered in clinical herpes from an isolated crop of vesicles to a fulminating illness with visceral necrosis. Recurrent infection occurs in individuals with circulating antibody and is usually localized. Both primary and recurrent herpetic infections of the outer eye can occur, the

former either as an isolated infection or an extension of a generalized infection. The diagnosis can be confirmed in the laboratory by examining vesicle fluid for characteristic cytologic changes, by isolation of the virus in laboratory animals, and by serologic tests for antibody. Primary infections are accompanied by an increase in antibody titers but little change can be detected in recurrent infections. The virus is not affected by any antibiotics or chemotherapeutic agents.

In discussing the clinical aspects of ocular herpetic infections, Goldsmith said that clinical cases of herpes simplex, as seen in ophthalmology, are largely recurrent manifestations of the disease. Cutaneous lesions are commonest around the mouth and nose. The onset may be precipitated by fever, exposure to sunlight, gastro-intestinal upsets, and menstruation, while other factors such as allergy and psychologic upsets have been implicated. Lid margin lesions are not uncommon. These may spread to the conjunctiva, but there appears to be no tendency for an eruption of vesicles to give rise to a contact infection of the cornea. Lid and conjunctival eruptions may be treated with any suitable ointment at night and antibiotic drops to prevent secondary infection. Local radiotherapy, vaccination six to eight times at weekly intervals with vaccinia calf lymph, and psychotherapy are measures that have been advocated for prevention of recurrent eruptions.

The onset of corneal lesions, as the dendritic ulcer, often accompanies a cold or upper respiratory infection and is occasionally preceded by mild local trauma. Local atropine to relieve discomfort and antibiotics to prevent secondary infection are indicated therapy. No known antibiotic or chemotherapeutic substance has any specific lethal effect on the herpes virus, and the only way to eliminate it is to destroy the epithelial cell in which it is living. Pure carbolic acid, strong tincture of iodine, the application of solutions of urea of bile salts, and the use of abiotic light may accomplish this effect. Topical cortisone is contraindicated.

Metaherpetic ulcers may follow the aforementioned lesions. Here there is a diffuse breakdown of the corneal epithelium without the characteristic branched staining pattern, occurring usually in cases where the original dendritic ulcer has been severe and long lasting, where there is already a corneal nebula, and when corneal sensation is poor. Numerous relapses may occur, with progressive scarring of the cornea. Most promising treatment is radiotherapy giving not less than 400 r of x-rays of 400 rep of beta rays spaced over four treatments at intervals of about a week. This may be of benefit in resistant primary dendritic ulcers as well.

Disciform keratitis and superficial punctate keratitis may be of herpetic origin, but the evidence does not tend to corroborate this.

In herpes zoster the pathologic process involves the sensory ganglion as well as the end organ. The offending virus is different from that of herpes simplex. In herpes zoster of the ophthalmic division of the fifth cranial nerve, involvement of the nasociliary branch usually precedes the development of ocular complications. The main changes in the eye are seen in the corneal stroma, iris, and ciliary body. Therapy is directed at preventing secondary infection. Cortisone may be of value. Postherpetic neuralgia is a difficult complication. The author advises prolonged barbiturate sedation and early return to normal activity.

In discussing radiation therapy of herpetic lesions, Lederman said that, as far as is known, radiation in therapeutic doses is not lethal to the organisms responsible for bacterial or viral inflammations customarily treated by this method. The precise mode of action of radiation on inflammatory processes is also unknown. Three mechanisms that may play a role are: (1) The possible stimulation of antibodies; (2) an effect on the cellular elements of the inflammatory exudate, particularly the leukocytes; (3) an effect upon the blood vasculature, especially the capillaries.

Radiotherapy can be applied to an inflammatory process to achieve the following clinical effects: (1) To reduce vascular engorgement and congestion accompanying inflammation, and to eradicate unwanted blood vessels; (2) to relieve pain; (3) to promote healing by assisting the resolution of the inflammatory exudate; the epithelialization of an ulcerated area, and the organization and removal of granulation tissue. Since the reason for its use in herpetic lesions is so vague, radiotherapy was used only as a last resort. Its use should be without hazard to the patient.

Table I shows the purpose, region treated, and radiation used for the various herpetic lesions.

The Phillips apparatus operating at 45 kv. was used for low voltage therapy. A radium source or a radioactive strontium source was used for beta radiation.

Low voltage therapy is always used for an acute or extensive lesion. The radiation is applied directly to the closed eye so that the whole of the outer eye and the eyeball are irradiated. The dosage is 10 r given once or twice a week for four weeks. This small dose will be effective if anything will; it is safe and may be repeated two or three times a year if necessary.

Beta radiation is reserved for chronic lesions, chiefly affecting the cornea, and single doses of 500 r are given weekly for four weeks. The two methods may be used in various combinations.

High voltage radiation (220 kv.) is used to relieve postherpetic neuralgia in herpes zoster ophthalmicus. Single doses of 150 to 200 r are delivered to the ipsilateral gasserian ganglion weekly for four weeks.

TABLE I

Radiation Therapy

Lesion	Purpose	Region Treated	Radiation Used
Dendritic ulcer	To promote epithelialization and healing	The ulcer	β
Disciform keratitis	(1) To relieve symptoms	The whole eye or the cornea	Low voltage therapy + β
	(2) Preoperative devascularization of cornea	The vessels entering the cornea	β
Postherpetic rash	To relieve pain	Gasserian ganglion	High voltage therapy
Superficial punctate keratitis	To relieve symptoms	The whole eye	Low voltage therapy

TABLE II

Results of Radiotherapy

Case	Seen	Treated	Relieved	Improved	Failed
Dendritic ulcer	22	20	3	10	7
Disciform keratitis	17	16	3	7	6
Preoperative	10	10			
Post-herpetic pain	11	11	2	3	6
Superficial punctate keratitis	73	68	12	44	12

Complications of radiotherapy such as exacerbation of symptoms, infection, and trauma are due to improper dosage and technique and may be avoided. The author has had no cases of radiation cataract with the dosages recommended. A summary of his cases is shown in Table II.

Comment: This series of three articles on herpes infections of the eye is well worth study by those wishing an up-to-date review of the subject. The material is factual, brief. and reflects much of the current knowledge and some of the fallacies.

Dudgeon refers to the work of this reviewer and his co-workers, in which local tissue immune factors were shown to play a large role in herpetic infections of the cornea, whereas humoral antibodies had only a minimal effect on epithelial lesions in nonvascularized corneae. He overlooked a parallel study on vaccinial keratitis (Speakman and Ormsby, 1954), in which intravenous hyperimmunization with vaccinia virus did not alter the corneal reaction to inoculation with this virus, whereas subconjunctival inoculation with attenuated virus completely protected the cornea from a subsequent inoculation. He correctly concludes (in the reviewer's opinion) that local tissue immune factors account for the attenuation of the virus after a certain period of activity, resulting in inability to recover virus from long-standing ulcers of the cornea, in spite of the clinical appearance of continuing activity.

If, as has been repeatedly demonstrated in our laboratory, it is impossible to recover virus from a high percentage of these chronic (metaherpetic) ulcers, one wonders if repeated cauterizations in such cases are not more damaging to the tissues than they are helpful in destroying virus. Possibly the chronic erosions and ulcerations are neurotrophic in type, due to destruction of corneal nerves. Lamellar keratoplasty in such cases was not mentioned in this review, but has worked well in our hands.

Smallpox vaccination for dendritic keratitis has little to recommend it. I have witnessed the development of a dendritic ulcer in the previously uninvolved eye of an individual who was receiving weekly vaccinations for a recurrent herpetic ulcer in the other eye.

I have not personally used radiation in herpetic keratitis and would hesitate to recommend it. Goldsmith's dosage of "400 r of x-rays or 400 rep of beta rays spaced in four divided doses at intervals of about a week" is half the cataractogenic dose of 800 r x-rays (Cogan) but well within the cataractogenic dose of 2500–3500 rep of beta rays. Danger would arise if such dosage should be repeated with subsequent attacks of the disease. It would be well for ophthalmologists to review thoroughly the literature on the complications of radiation therapy before deciding upon this hazardous, and probably useless procedure.

HUGH L. ORMSBY

THE INTRAOCULAR PRESSURE

MALIGNANT GLAUCOMA

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Am. J. Ophth., 1957, *43:* 388–399

The concept of malignant glaucoma today is based on the mechanical classification of glaucoma into narrow-angle and deep-angle glaucoma. Failures in the surgical management of malignant glaucoma have been widely reported, not only for one, but for both eyes. Inquiry into the origin of the syndrome therefore seems advisable. Malignant glaucoma, as a mechanical problem, does not entirely fit into the present-day classification of glaucoma. Blocking of the trabecula after surgery for subacute angle-closure glaucoma is apparently due to causes of more than a mechanical character.

Chandler (1950) described malignant glaucoma as "a form of postoperative glaucoma, in which, after any anterior operation for glaucoma, the anterior chamber remains, or shortly becomes, flat and the tension rises. . . . It apparently occurs in approximately two per cent of the cases and is seen only in eyes with a shallow anterior chamber and an elevated tension at the time of operation." He further states that the "essential feature of the condition is a forward displacement of a relatively large lens." This is the mechanism by which malignant glaucoma develops. From this it can easily be seen that the classification of glaucoma on the basis of gonioscopic findings alone has led to the neglect of several important factors. One of the most important of these is the lens. While malignant glaucoma is certainly a form of narrow-angle glaucoma, the exciting cause in many cases is a lens that is too large for the eye. Small eyes have been observed in several patients with malignant glaucoma and the fact that glaucoma is more to be dreaded in small hypermetropic eyes has long been accepted. Malignant glaucoma, however, is not always found in small eyes; patients with enlargement of the lens as a result of advanced age, an earlier operation, or other causes may also be affected.

Although it is generally agreed that an extremely shallow anterior chamber and a high preoperative tension predispose a patient to malignant glaucoma, a complete picture of the disease cannot be obtained without a consideration of several other factors, notably (1) neglect or errors in judgment; (2) pupillary block by the lens (not by peripheral anterior synechiae); (3) heredity; (4) emotional stress or nervous tension; (5) vascular disease, including that associated with diabetes; (6) vitreous disorders; (7) intumescence of the lens; (8) relation to chronic glaucoma; (9) a flat anterior chamber after operation; (10) acquired myopia in glaucoma; (11) the size of the lens and of the eye; (12) the other eye;

and (13) multiple operations. Anything that aggravates either the pre-existing glaucoma or the further enlargement of the lens leads rapidly downhill. Treatment must produce simultaneous relief of both of these conditions. If, for any reason, only one can be controlled, it should be the enlargement of the lens. Treatment of lens enlargement alone has often proved successful, while treatment of glaucoma alone has more often failed.

Emotion is conceded to be a factor in the pathogenesis and progress of all forms of glaucoma. Emotional trauma and stress aggravate the glaucomatous component in malignant glaucoma and, since the instability of the glaucomatous eye is not controlled by surgery, the prognosis in many cases of glaucoma complicated by emotional disorders is poor.

Recognition, in patients with glaucoma, of the importance of the lens and of the existence of two separate pathologic processes which together produce malignant glaucoma will tend to simplify the preoperative diagnosis. The factors that lead to malignant glaucoma in one eye are also to be expected in the other eye. Lenses behave similarly. They grow at the same rate, and they often degenerate at the same rate. Eyes are usually of the same size. The ratio of the lens to ocular volume is essentially the same in each eye. Heredity and emotional factors will have the same effect on each eye. Astute diagnosis requires the examiner to be on the alert for factors that disturb the similarity of behavior of the two eyes. In most cases, however, because the second eye usually follows the course taken by the first eye, the proper treatment is lens extraction. Concern must be felt for the second eye even during the acute phase of the disease in the first eye. Complete diagnosis, proper sedation, both at home and preoperatively, and the value of general anesthesia in certain cases must be emphasized in relation to the best management of the second eye.

The term clear lens places too much emphasis on an unimportant point, whereas attention should be focused on the simultaneous occurrence of the syndrome of narrow-angle glaucoma and the presence of an enlarged lens. When these coincide, malignant glaucoma is present, and the clearness of the lens, or its opaqueness, does not alter the need for its removal. If the term clear lens is to be used, it should refer to the stage of prodromal malignant glaucoma, before the acute rise in tension has occurred and when the lens can be observed to be clear. Removal of the lens is indicated in prodromal malignant glaucoma, regardless of the stage of the lens, because glaucoma surgery alone will result in the onset of malignant glaucoma. Lens extraction may, however, be combined with other operations if the blockage of the angle is great enough to require a filtration channel.

Failure to control glaucoma by glaucoma surgery alone suggests (1) neglect on the part of the patient; (2) unavoidable surgical complications; or (3) an incomplete diagnosis. In both malignant and prodromal malignant glaucoma the operation of choice is lens extraction combined with a filtration procedure performed at the same time to avoid repeated operation. The operation is indicated when tension begins to be uncontrollable, e.g., when pilocarpine of more than 4

per cent solution is required at 2 hour intervals or less. Prophylaxis against malignant glaucoma in each eye requires the diagnosis of prodromal malignant glaucoma to be made on the first eye and not the second. Proper treatment of the first eye may prevent or postpone surgical intervention in the second eye, even in the presence of long-standing chronic narrow-angle glaucoma in the aged.

Comment: This commentator, being prejudiced, perhaps, in his views regarding the importance of the so-called gonioscopic classification of glaucoma, considers it necessary to refute some of the premises held in this interesting article. First of all, malignant glaucoma is not a specific form of glaucoma but rather a postoperative complication of certain forms. It occurs most often after angle-closure glaucoma but may occur rarely after filtering operations for chronic simple glaucoma in eyes with shallow anterior chambers. The cause is forward displacement of the lens but I disagree that it need be a relatively large lens, but rather a disturbance of the lens suspensory ligament. Let us consider that stretching or tearing of the zonule could allow the lens to come forward and cause pupil and trabecular block.

I agree with Birge that age, and intumescence of cataract can increase the lens size but in those lenses which I have removed for this condition the lenses were clear and not larger than would be expected for the age of the patient. It is true that the lens is relatively large in those cases with microcornea and may be considered as relatively large in all small eyes. However, only a small number of these cases occur and all patients with microcornea and angle-closure glaucoma do not develop malignant glaucoma.

To digress for a moment, Birge states that "it has long been accepted that glaucoma was more to be dreaded in small hypermetropic eyes." This statement requires elaboration. One must consider the type of glaucoma; in chronic simple glaucoma the refractive error has no significance whatever, but in angle-closure glaucoma hyperopia is the usual manifestation of the smallness of the eye and is extremely important.

The removal of the lens should be made after an *ab externo* incision with several corneoscleral sutures. Whether one finds posterior sclerotomy necessary varies with the surgeon. Even though an iridectomy has already been made during the primary glaucoma operation, a broad basal iridectomy should be done and a cyclodialysis spatula used to tear any synechias in the angle (the Chandler maneuver). The lens usually pops forward on opening the eye and indicates that the zonule is torn.

I believe that the only way one may prevent malignant glaucoma is to avoid rapid evacuation of the anterior chamber. Otherwise I do not believe prevention in the first eye to be possible. However, since the same cause of zonule weakness is probably present in the second eye, prophylaxis of the second uninvolved eye in angle-closure cases may be and should be accomplished by doing a peripheral iridectomy through a flap-covered, sutured small incision. This may be done at the time of the lens removal on the first eye.

H. Saul Sugar

CONSIDERATIONS ON MECHANISM OF ACTION OF CYCLODIALYSIS

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Boll. ocul., 1956, *35:* 401–411

Many theories have been advanced to explain the hypotony-producing mechanism of cyclodialysis. The hypothesis of a mutilating action and of a reduction in the secretion of aqueous humor through the destruction of a part of the ciliary body has been discarded. Recent histologic and gonioscopic studies of eyes in which cyclodialysis was successful indicated that dehiscence of the ciliary body is necessary if the hypotensive effect is to be present. Kleinert's hypothesis that cyclodialysis creates, independently of the suprauveal space, new paths of outflow (anastomosis of Schlemm's canal with the ciliary veins) has not been sufficiently proved. The latest studies with modern methods of investigation ascertained that cyclodialysis acts mainly by causing a marked diminution (reversible) in the secretion of aqueous humor for varying periods of time.

The characteristics of cyclodialysis are discussed briefly by the author who announces an extensive comparative study between this and other types of antiglaucomatous operations.

(1) In cyclodialysis the mechanism of reabsorption of the fluid through the suprachoroidal space is in essence different from the mechanism at work in normal conditions or in other types of antiglaucomatous interventions. In these the difference of hydrostatic pressure between eye and episcleral venous system is important, whereas the pressure in the choroidal veins depends entirely on the intraocular pressure and any increase in this results in an increase in the drainage venous system. As a consequence, the outflow, which is automatically governed by the ocular tone in normal conditions and in other antiglaucomatous operations, becomes independent of the ocular tone in cyclodialysis.

(2) Cyclodialysis, more than any other type of operation, seems to reduce markedly and lastingly the production of aqueous humor. This is explained by the author by the fact that in no other intervention does the aqueous humor come in contact with a vast vascular bed of the thin walls: because phenomena of diffusion prevail over those of secretion, any difference of concentration at the two sides of the hemato-ophthalmic barrier tends to be abolished together with the hypertony of the intraocular fluids. In these conditions the various components of the aqueous humor pass through the hemato-ophthalmic barrier with a velocity that is in inverse proportion to their molecular weight.

Although no data are as yet available on the crystalloid osmotic pressure of the aqueous humor in eyes subjected to cyclodialysis, in these eyes such pressure is closer to the plasma pressure than is the same pressure in eyes subjected to other antiglaucomatous operations. Thus one of the main factors that ensures the circulation of the intraocular fluids is eliminated. The condition is analogous to

that present in uveitis and in retinal detachment where, together with hypotony, there is also a reduction of the flow of the aqueous humor. Consequently it can be assumed that in the suprachoroidal space only colloid osmotic forces are acting from the interior of the eyeball toward the hematic environment with an inverted direction of the normal fluid flow at the level of the anterior uvea.

The opening of a new path of outflow with lower resistance can lead to obliteration of the normal pathways as is proved by those cases of eyes subjected to cyclodialysis in which the sudden closure of the filtering scar can lead to a dramatic increase of pressure with high resistance to outflow, to values greater than the preoperative ones. In some other cases the closure is gradual and the preoperative values are restored slowly. This indicates that in the presence of a filtering scar the eyes in the end will depend entirely on the existence of the scar. In cases in which the hypotony is more marked an outflow of the aqueous humor through the path of the episcleral veins must be considered impossible because the pressure in this drainage system is higher than the intraocular pressure and therefore the "outflow pressure" assumes negative values.

The author reports on four cases of hypotony following cyclodialysis in which results of Blaxter's bulbar pressure test and of Weekers and Delmarcelle's test indicated that the above hydrodynamic peculiarities were present. Besides abnormal hypotony, stasis of the intraocular fluids and a marked resistance to outflow were present, and the scarce exchange with the hematic environment took place exclusively through the suprachoroidal space. In the one patient in whom the hypotony was extremely marked, it was ascribed to an exaggerated hypotony-producing mechanism of cyclodialysis. On the basis of the biomicroscopic and goniometric examinations, the author concedes that in this case a repeated cyclodialysis could have destroyed a large part of the ciliary body in an eye that showed congenital defects of the secretory part of the uvea. However, he feels that the most plausible hypothesis is one that assumes a causal relationship between the hypotony and the existence of an abnormally wide suprauveal fistula and the presence of fine fibrous branches of the vitreous incarcerated in the iridocorneal angle. Even so, it is difficult to explain why this, which in general is considered a much-feared hypertensive complication, can, in some cases, have the opposite effect.

Comment: As with all hypotheses in regard to the *modus operandi* of cyclodialysis, to date no positive evidence has appeared to settle the problem. Although fluorimetry and tonography indicate a decrease in aqueous formation for a time after the operation, this is uncertain, especially since no definite knowledge is available as to the venous pressure changes under the conditions of hypotony. The author's use of Blaxter's and Weekers tests cannot be considered as conclusive. After the initial period, pressure remains low, apparently directly related to the presence of the opening to the suprachoroidal vessels. Anything which closes the cleft will return the tension to its elevated level, thus indicating that there is no relation between possible atrophy of the ciliary body and the lowering of tension.

It occurs to me that no one has compared the vascular exchange into the eye at the ciliary body with the outward exchange at the suprachoroidal vascular barrier. We need to know more of the osmotic and chemical exchanges at the latter site.

H. SAUL SUGAR

THE LACRIMAL SYSTEM

EPIPHORA: ITS RELATION TO THE ANATOMIC STRUCTURES AND SURGERY OF THE MEDIAL CANTHAL REGION

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Tr. Pacific Coast Oto-Ophth. Soc., 1956, *37:* 31–46

The cure of epiphora is dependent upon a knowledge of the structures of the medial canthal region, and good results in handling problems of the lacrimal drainage system will be in direct proportion to an understanding of its mechanism. The anatomic relationships of this area are intricate, and misconceptions of some of the structures have crept into the textbooks.

In an earlier report on this subject, several observations were made on what were termed the "lacrimal diaphragm" and the "lacrimal pump." Parts of that report must now be clarified and revised on the basis of additional study and dissections. Encouraging results have also been obtained in further clinical experience.

Observations in 10 orbital dissections carried out in the department of anatomy, University of Oregon Medical School, have shown that the medial palpebral ligament consists of an anterior part and a posterior part. The anterior part gives rise to all the superficial heads of the orbicularis oculi muscle. The posterior part gives rise to two previously undescribed muscles which are the deep heads of the preseptal muscles. The lacrimal diaphragm consists of the periorbita covering the lacrimal fossa which is blended in its upper half with the posterior part of the medial palpebral ligament. The lacrimal pump, which is present in each lid, consists of, first, the superficial and deep heads of the pretarsal muscle; second, the deep head of the preseptal muscle; and third, the lacrimal diaphragm.

The factors involved in moving the lacrimal fluid from its entrance in the upper conjunctival cul-de-sac to the floor of the nose may be summarized as follows: (1) In the conjunctival sac: linear strips or tears form along the palpebral margin of each lid and are forced to flow medially, not only by the medial movement of the lids, but also because in blinking the lids close progressively from the sides to the center. (2) In the canaliculus: capillary attraction, as well as compression and shortening of the ampulla and canaliculus, conducts the tears toward the tear sac. (3) In the tear sac: alternate negative and positive pressure produced by movement of the lacrimal diaphragm first draws the tears into the sac and then expresses them into the nose. Negative pressure in the nose during inhalation, snuffing, and gravity are also factors in emptying the sac. From this summary it can be seen that the movement of tears is most dependent on the structures termed the lacrimal pump. Instead of being confined to the lower lid,

as first reported, it is now evident that the pump also functions in the upper lid. The anatomic concept of a lacrimal pump appears to settle the century-old controversy as to whether negative or positive pressure is created in the tear sac by blinking. It seems logical to assume that for maximum efficiency the pressure in the sac should be negative at the same moment the canaliculus is shortened and compressed. This is exactly what the lacrimal pump accomplishes, as shown by the clinical observation that mucus in fistulas and intranasal windows recedes into the sac during the act of blinking.

Certain points deserving of comment have emerged from further clinical experience with conjunctivodacryocystostomy, conjunctivorhinostomy, and surgical measures for the repair of injuries in the medial canthal region. The first two conjunctivodacryocystostomies, in which the Stallard method was used, were failures, apparently because the stab wound in this procedure comes out inferior and lateral to the lower Horner's muscle so that all of its important pumping action is lost. The conventional cutaneous approach to the sac was used in these two cases. In the next seven, the conjunctival approach proposed in the earlier report was used. In the tenth case, the fact that the tissue had been badly distorted by a previous accident forced a return to the cutaneous approach. This approach simplifies the procedure by allowing easier exposure of the sac, with less danger of perforating the sac in dissecting the fundus free, and less tendency for the ostium to migrate upwards and away from the lacrimal lake postoperatively—a complication which occurred in two cases.

In general, it is best to treat the tear sac in its periosteal envelope. Without the periosteum the tear sac mucosa is so friable that suturing is difficult. In operations requiring mobilization of the fundus of the sac it is best to separate the medial periosteal wall of the sac from the bone of the fossa and then to dissect carefully between the lateral periosteal wall (lacrimal diaphragm) and the deep muscle heads until the fundus is free. It is important not to injure Horner's muscles. The next step is to make a clean stab wound with a sharp pointed knife. The wound should be about 10 mm. long and extend from the conjunctival side between the parallel to the superficial and deep heads of the pretarsal muscles. The fundus of the sac is then split anteroposteriorly, pulled into the stab wound, and sutured to its margins with 5-0 mild chromic gut. The sac and ostium are packed with vaselined umbilical gauze tape. This is removed on about the 10th postoperative day. If it is necessary to keep the ostium from narrowing after the packing has been removed, the patient can be taught to use the large end of a Ziegler double-ended needle for daily dilatation. The clinical results in the 8 operations done by the new technique were good in 6, fair in 1, and poor in 1. In each case this procedure was necessary because both canaliculi had been destroyed.

Four patients were subjected to conjunctivorhinostomy, two by the external and two by the intranasal approach. One had had a previous dacryocystectomy, two had had other unsuccessful attempts to establish drainage followed by a dacryocystectomy and one had a congenital absence of the entire lacrimal drainage apparatus. The intranasal approach is the same as that outlined in the pre-

vious report, but the external approach, which is described in detail, is new. All four patients have patent ostia and in three the epiphora has been relieved. In the fourth patient (with the entire lacrimal drainage apparatus lacking) the operation was performed too recently to make an evaluation of the results possible.

In repairing lacerations of the medial canthal region, it is necessary not only to strive for a cosmetic effect, but also to reunite the injured parts of the lacrimal apparatus. The principles by which this can be accomplished are set forth and the importance of postoperative immobilization of the lids is emphasized.

The data obtained in this study show that not all of the anatomic parts of the lacrimal drainage system need to be restored to cure epiphora. Not all of the parts of even the lacrimal pump seem to be indispensable. Relief of tearing may be attempted as long as there is some degree of medial movement of at least one id containing a functioning Horner's muscle.

Comment: In the first part of this paper the author presents an excellent review of the anatomy of the inner canthal area. Both the anatomy and the function of these structures are important to the proper understanding of the surgical procedures reported.

Although the problem of surgical repair of medial canthal injuries is well recognized, it is well to re-emphasize the problems involved, particularly the proper apposition of the severed canaliculus.

The results reported in conjunctivodacryocystostomy and conjunctivorhinostomy are certainly stimulating. The patient in whom such a procedure is indicated is indeed a problem and these procedures should probably be used more often. The techniques as outlined by the author should aid in accomplishing a better understanding and more frequent consideration of these procedures.

T. E. SANDERS

DACRYOCYSTORHINOSTOMY: RHINOLOGIC ASPECTS

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Acta ophth., 1956, *34:* 404–411

Dacryocystorhinostomy, as Toti introduced it, was first carried out by rhinologists using the external approach. Later, the intranasal procedure was devised and produced such good results that even ophthalmologists began to use it. In 1930, Loeffler reviewed the available literature and the statistics he published showed that the proportion of good long-term results obtained by both the external and the intranasal procedures was exactly the same, 84 per cent. It is, therefore, not surprising that more and more ophthalmologists themselves took

charge of cases requiring surgical treatment for dacryostenosis and dacryocystitis, and that the external method has predominated in the last few decades.

The question then arises, can intranasal dacryocystorhinostomy now be dispensed with? Ophthalmologists with whom this question is discussed often say that they have found the operation more difficult than they expected and that the final result has often been disappointing. The need for cooperation between ophthalmologists and rhinologists in the preoperative examination of the patients is generally recognized, and it may well be asked whether rhinologists should not again be employed more extensively for dacryocystorhinostomy. This applies, of course, especially to cases in which the ophthalmologist doubts his ability to perform the operation, but it is also a valid question when anatomic conditions make the intranasal procedure the more desirable one. Finally, it may be asked whether a rhinologist may not be able to render valuable assistance during the postoperative period following external dacryocystorhinostomy.

Cooperation between ophthalmologists and rhinologists has been satisfactorily established at the University Hospital in Helsinki. Dacryocystorhinostomies are performed at both the ophthalmic and the otolaryngologic clinics according to the nature and requirements of each case. An analysis of the results obtained in 124 intranasal dacryocystorhinostomies performed by the author since 1940 (104 for dacryocystitis and 20 for dacryostenosis without suppuration) revealed several points of special interest from the ophthalmologic point of view. The patients ranged in age from 6 to 64 years, and all had been referred for operation by ophthalmologists. At follow-up (from 6 months to 11 years after operation or last revision), 58 of the 62 patients treated in the period from 1940 to 1947 were traced; 34 had good results and 24 had poor results. Apparently, the symptoms had returned after the operation in many cases, usually within a few weeks, but in spite of this the patients had failed to come for revision, partly because of the abnormal conditions caused by the war. Since 1948, the results have been much better; all 62 of the patients have been seen and the results were good in 60 (97 per cent). These figures show the importance of following the patients and determining the effect of operation and the causes of failures when they occur. If it is simply assumed that the patients who do not return have had a good result, an entirely misleading impression will be conveyed and many a well-needed revision will remain undone.

In selecting patients for operation and in deciding whether to use the external or the intranasal procedure, certain points must be carefully considered. First the epiphora must be due to stenosis below the tear sac, that is, in the nasolacrimal duct. In addition, there must be adequate canalicular function. Consequently, patency of the canaliculi and a correct position of the eyelids must be determined. In doubtful cases a canalicular test should be made according to the method of West. These examinations should be carried out by an ophthalmologist because he can best appraise the situation. Evaluation of canalicular function is especially important in the case of aged patients. Experience has also shown that it is necessary in patients who have had prolonged epiphora without any suppuration in the lacrimal sac. In such cases, the epiphora may be due to

stenosis of the nasolacrimal duct, but this must be definitely demonstrated and the possibility of reduced canalicular function excluded before dacryocystorhinostomy is undertaken.

Preoperative examination of the nose is essential, partly to discover, if possible, the cause of the dacryostenosis and partly to find out whether there are deformities in the nose. The cause of stenosis in the nasolacrimal duct is surprisingly seldom revealed by rhinological examination—only in about 10 to 20 per cent of the cases. The examination must be made, however, and the cause discovered if it is nasal in origin. It will usually prove to be ozena, lupus, a tumor, or the sequel of trauma or operation.

Repeated observations support the belief that prolonged and intensive probing of the lacrimal passage may make it difficult to obtain good results by dacryocystorhinostomy. The place where probing most easily causes lesions and stricture seems to be the small common duct joining the canaliculi to the tear sac, which might very appropriately be termed the ductulus lacrimalis communis. Probing, if it is without effect, should not be continued beyond a certain time: dacryocystorhinostomy should be resorted to instead, unless contraindicated. It is a mistake to suppose that suppuration must be cleared before the operation is undertaken. On the contrary, it seems easier to obtain good results when operating on a suppurating tear sac. Postoperative treatment with revision is required more often in cases of so-called clear dacryostenosis than it is in dacryocystitis.

The intranasal procedure is the only possible one when the operation is required in phlegmonous dacryocystitis and the only correct one in the presence of severe deformity in the nose. It is preferable to the external in the following conditions: (1) If the dacryocystorhinostomy must be preceded by resection of the septum or of the anterior third of the middle turbinate—when this is so, the corrective measure and the operation on the tear sac can be performed at one session if the intranasal approach is used; (2) in fistulizing dacryocystitis; and (3) in the case of a recurrence after the external procedure.

The results obtained in ozena were poor. Lupus of the nose and sinusitis must be treated before dacryocystorhinostomy to avoid recurrence or closure of the opening. The postoperative contact between the surgeon and the patient is of the utmost importance. Even in the second group of patients postoperative measures were needed in no fewer than 20 of the patients before permanently good function was secured. Probing and removal of granulations were sufficient in some cases, but in others a more thorough revision was needed. Postoperative intranasal measures are also needed after external dacryocystorhinostomy in some cases and in these cooperation between the ophthalmologist and the rhinologist is essential.

Comment: The principal objective of this paper is an argument for the increased use of intranasal dacryocystorhinostomy. A secondary purpose is a plea for increased cooperation between the ophthalmologist and the rhinologist in the management of dacryocystitis, stressing an adequate rhinologic examination in any patient in which dacryocystorhinostomy is contemplated.

In this reported series of 124 operations, good results were obtained in only 59 per cent

of the original 62 cases, while 97 per cent successes occurred in the second group of 62. This difference in results would seem to indicate either a modification of technique, increased experience with the procedure, or better postoperative management. Nothing is learned from this paper regarding either the original technique or any modification, as operative technique is not mentioned. The author stresses the importance of careful and probably prolonged postoperative treatment as a factor in successful drainage. This may be a source of the unusually large percentage of cases needing revision (20 of 60 cases).

Good canalicular function as a prerequisite of a successful dacryocystorhinostomy seems obvious but the author's reiteration of this is well taken. As a rhinologist, the author's interest in the role of internasal pathology is natural, but this in itself is not a real argument for the intranasal approach. Such intranasal conditions can be recognized and treated prior to the external operation. However, the reviewer believes that routine dacryocystography to locate the site of block is just as much indicated as a preoperative procedure in either route. There would seem to be complete agreement between the author and American authorities as to the superiority of a successful dacryocystorhinostomy by either route over extirpation of the sac.

The statement that only 10 per cent of dacryocystorhinostomies in this country are done by the intranasal route is possibly correct as these patients usually present themselves to an ophthalmologist. In a rather infrequent procedure, this would leave only a very small number of cases available to the rhinologist. From the author's own experience this would seem to be an insufficient number for any rhinologist to become expert in that procedure. This procedure apparently has been developed by the ophthalmologist, not only from his greater experience with lacrimal sac diseases, but also out of necessity as rhinologists are not trained in the technique. If the intranasal technique is so difficult, it would seem that the modern external operation with its adequate exposure of the sac and direct suturing is a superior procedure of the inexperienced operator.

The superiority of the external approach would seem to be suggested by the author's own evidence: the necessity of long experience in the technique of the intranasal route, the need for careful postoperative management, and the high percentage of revisions.

T. E. Sanders

SUMMERSKILL'S DACRYOCYSTORHINOSTOMY

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Brit. J. Ophth., 1957, *41:* 111–114

Drainage of obstructed lacrimal sacs through the lacrimal bone into the middle meatus of the nose has for years been achieved by the time-consuming operation of Toti and its modifications. In 1952, however, the work of Summerskill showed that excellent drainage can be achieved and maintained by the simplest of methods. His operation, which represents a great advance over any other previously published procedure, has certainly not received the attention it deserves.

Experiments with this method have been under way at the C. M. S. Hospital since 1953 and the results obtained have been almost consistently good. The operation offers so many advantages in speed, simplicity, and effectiveness that the present small series of cases is published in the hope of increasing acceptance of the procedure.

Summerskill's method, slightly modified, was used in 36 consecutive cases of nasolacrimal obstruction operated on at the annual eye clinics in Shikarpur and Khairpur, Pakistan, in January, February, and March, 1955. The patients fell into two groups, those with lacrimation and a mucopurulent discharge on pressure over the inner canthus and those with fistulae which had been discharging mucus or mucopus for months or years. There were 29 patients in the first group, ranging in age from about 2 or 3 to 50 or 60 years (since many of these people of the poorer class have no idea of their age, ages must be approximated). Patients in the second group numbered 7, and all had excess fibrous tissue around the sac, together with some overlying edema due to recent inflammation.

The method used followed Summerskill's technique as described by him in 1952 in all essentials, except that the opening into the nose is made by a trocar and cannula and that the only sutures inserted are those into the skin. In place of a long and extensive procedure, the whole operation can be completed with a speed that will astonish the operator himself. Once the simple steps used in identifying and opening the sac are mastered, the insertion of the tube and the stitching of the wound can be done very quickly. As soon as anesthesia is established and the field prepared, it has been found that the total time taken for the operation in 80 per cent of the cases varies from 3 to 5 minutes. This fact alone commends the procedure for use in Pakistan, where it was necessary to perform an average of over 40 cataract extractions and over 20 other major ophthalmic operations daily for two weeks in one of the clinics in 1955. The early results of the operation were most pleasing to patient and operator alike. The symptoms were immediately relieved and the wounds healed quickly. It is too early to comment on the long-term results except to say that only about 12 of more than 100 patients with lacrimal obstruction operated on since 1953 have returned with a recurrence of symptoms, and all but one of these had been operated upon by beginners. The mishaps were all caused by a displacement of the polyethylene tube, and all were successfully corrected by reoperation. The patients themselves were impressed by the little discomfort they suffered; in more than 90 per cent of the patients discomfort was hardly noticeable and even those few with surrounding inflammation or fibrosis before operation who did complain of slight pain rarely needed sedatives.

OPERATIVE PROCEDURE

The nasal cavity on the appropriate side is packed with gauze impregnated with local anesthetic and 1:1000 epinephrine in equal parts ten min. before the operation. Anesthesia is by means of local infiltration and block of the nasolacrimal nerve. Operations in children are performed with intratracheal ether anesthesia. A vertical incision is made 3 mm. medial to the inner canthus and

the skin and obicularis muscle are retracted. The lacrimal fascia is incised and dissected off the sac which is opened and its mucoid or mucopurulent contents swabbed out. A trocar and cannula of suitable size are passed through the lower end of the medial wall of the sac and on through the lacrimal bone and into the nasal cavity in one motion. The instrument is then removed and the polyethylene tube, mounted on a simple introducer, is passed through the hole so that the tip of the tube rests firmly against the medial wall of the sac. The sac is not closed but the skin is closed with silk sutures which are removed on the sixth postoperative day.

Comment: Any dacryocystorhinostomy that can be done in eight to ten min. with a high percentage of successful results certainly deserves careful consideration of all ophthalmic surgeons. If this technique is effective the author's statement that "the operation has certainly not received the attention it deserves" is surely true.

From the technique described and the results reported in this paper, it would seem obvious that further trial of this operation is indicated. It would seem feasible to the reviewer that after the tract is epithelialized the tube might be removed by the intranasal route. This would eliminate any foreign body reaction that might occur over a long period of time.

T. E. SANDERS

NEUROLOGY

ON CERTAIN HISTOLOGICAL AND RADIOCLINICAL FORMS OF NEUROFIBROMATOSIS

Reboul, Bessière, Léger, Mme J. Chabot, Delorme, and Fau

Bull. Soc. opht. France, 1956, 831–836

The clinical and histologic polymorphism of neurofibromatosis (von Recklinghausen's disease) was well illustrated in seven patients with varying clinical manifestations of the disease, some of which involved the orbit. The cutaneous and nerve tumors and pigmented spots that constitute the symptomatic triad of neurofibromatosis are sometimes accompanied by endocrine and psychic disturbances and by changes in the bones, especially those of the skull, the vertebral column, the thorax, and the limbs. Polycystic neurofibromatous areas may appear in the bone tissue; lacunae in the cranial vault and destruction of the base, the sella turcica, the upper edge of the petrous portion of the temporal bone, and the occiput in the neighborhood of a subdermal neurofibroma may be due to fibrous metaplasia; and the presence of a nearby tumor may be responsible for destructive erosion of the bone. In addition, perforation of the orbital wall, especially the upper wall, sometimes leading to endophthalmos or pulsating exophthalmos, has been reported in some cases.

The tumors of neurofibromatosis are generally benign and their development is usually very slow. Metastasis is rare, but the tumors almost always recur after simple ablation. Anatomically, they develop at the expense of the cells of the sheaths of Schwann or of the conjunctival cells of the fibrous nerve sheaths. Mixed forms are sometimes found. Clinically, the tumors may be central, characterized especially by lesions of the neuraxis, or peripheral. Plexiform palpebro-orbital neuromas, schwannomas of the eyelid, and neurinomas of the orbit are among the peripheral forms most commonly described.

The clinical manifestations of the disease found in the authors' patients were: Patient 1, the typical cutaneous form, with strawberry-like pedicled tumors appearing over the whole of the body; Patient 2, typical cutaneous lesions associated with a neurinoma of the pneumogastric nerve; Patient 3, a histologically mixed tumor (neuroschwannoma of the eyelid); Patient 4, an extensive neurofibroma of the orbit and numerous bone changes, including destruction of the orbital floor; Patients 5 and 6, cutaneo-osseous neurofibromatosis with malignant degeneration; and Patient 7, signs of cutaneous neurofibromatosis dating from childhood coupled with recent impairment of a previously good general condition as a result of pleural effusion and polycystic tumor masses that appeared to be intrapleural.

Although the development of the disease was prolonged in some of these patients, several decades having been required for its progression to the monstrous

orbitofacial deformities found in Patient 4, in others it pursued a rapid pseudomyelomatous course.

The findings in these patients emphasize the possibility of diffuse bone lesions, often with serious ocular repercussions, and the comparative frequency with which malignant complications may be encountered.

Comment: It is likely that the authors' concern over the relative frequency of malignant degeneration in the tumors of neurofibromatosis is the result of the higher incidence of such change in their series of patients reported. Reese in his book, *Tumors of the Eye*, states that a local malignant tumor may occur at any involved site with blood stream metastasis, and that the tumor is usually a malignant schwannoma. He quotes one author who stated that such malignant change occurs in 13 per cent of cases with von Recklinghausen's disease, but notes that other authors have pointed out that such a figure is definitely too high, since many routine cases of multiple neurofibromatosis are never reported to weight the series against malignant breakdown.

The occurrence of bony cranial defects in this group of patients must be kept in mind whenever the differential diagnosis of pulsating exophthalmos is made. Characteristic of such an orbital defect is pulsation of the globe, unaccompanied by bruit, and with no discomfort complained of by the patient. Of course, many patients will show the other stigmata of von Recklinghausen's disease if the examiner will take the trouble to check the general physical findings.

The association of gliomas of the optic nerve with this disease must be remembered, since again the signs of café au lait spots, subcutaneous neurofibromatous nodules etc., will be helpful in the differential diagnosis.

One rare situation with neuro-ophthalmologic interest is the occurrence of bilateral acoustic neurinomas in patients with von Recklinghausen's disease. Fortunately these are rare, since the morbidity of bilateral surgery, with resultant bilateral deafness, is a problem which the neurosurgeon hesitates to face.

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INFANTILE OPTIC ATROPHY

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Tr. Ophth. Soc. U. Kingdom, 1956, *76:* 127–135

The question of partial optic atrophy in a particular infant will often remain unsettled unless and until the patient reaches the age and the level of intelligence to perform subjective tests, including perimetry. Sometimes optic atrophy will be foreshadowed by external signs of ocular abnormality, such as nystagmus, impaired pupillary reactions, a blank stare, proptosis, or squint. It may be linked with other fundus lesions. One may be led to scrutinize the disks by reason

of head injury, mental retardation, or maldevelopment of the skull as well as in routine examinations.

OPHTHALMOSCOPIC SIGNS

Disk pallor, the cardinal sign of optic atrophy, is common to all types, but there is no precise ophthalmoscopic criterion of pathologic pallor.

(a) Primary optic atrophy is applied especially to degenerative diseases. However, inflammatory lesions far behind the nerve head can produce exactly the same picture. Other features are clear cut disk margins, deepening and perhaps enlargement of the physiologic cup, occasional slight recession of the whole disk, and in some long standing cases the retinal vessels are attenuated.

(b) Secondary optic atrophy as discussed here is a sequel of disk edema, whether from increased intracranial pressure or retinopathy. Slurring of the margins and obliteration of the physiologic cup are characteristic features.

(c) Consecutive destruction of nerve fibers, as happens, for example, after choriodoretinitis. The disk appearance resembles partial atrophy of the primary type.

(d) Glaucomatous optic atrophy, although uncommon among infants, is an important type. Progressive rise in the intraocular pressure will gradually enlarge and deepen the cup, and during intermediate stages cupping will be essentially pathologic although incomplete. By the time a glaucomatous cup has spread to the disk margin the infant's affected globe will also have suffered distention.

FALLACIES AND DIAGNOSTIC OBSTACLES

The inadequacy of pallor as a quantitative index of atrophy is emphasized. There is a wide range of disk color within normal limits, and disk pallor can far transcend the usual range of variation without necessarily signifying atrophy. Also, the average infant's disks are paler than those of older children and adults. Since myelin is essential for the conduction of light sensation, delayed myelination will result in prolongation of the newborn's blank stare and must be borne in mind.

An actual hypoplasia may account for apparent optic atrophy. Gross developmental defects usually reduce the disk diameter, but minor faults are compatible with a normal sized disk. Unilateral myopia is an important reason for unilateral disk pallor in an infant.

Obscuration of the physiologic cup can be a useful corroborative pointer to secondary optic atrophy, but is in many cases a harmless phenomenon due to a congenital variation. Unless there are corroborative signs of disease, it is unwise to interpret blurred margins pessimistically.

TREATMENT

Infantile optic atrophy is not usually amenable to direct therapy, although its presence will sometimes help to decide whether treatment is needed for associated lesons elsewhere in the body.

SIGNIFICANCE OF OPTIC ATROPHY

Questions of prognosis and disposal loom far larger than those of treatment for infants afflicted with optic atrophy. Due to the difficulties in diagnosing partial optic atrophy, prognosis must often be guarded. When once optic atrophy is established, one cannot expect it to resolve, whether it be partial or complete. One must remember that an intelligent child with optic atrophy will utilize his other special senses maximally and may develop at such a rate as to lead one to believe his optic nerves had actually improved.

The disposition of each case is a highly individualistic one. Variations in environment and the incidence of other associated handicaps make generalizations impossible. Temporizing is in many instances not only legitimate but desirable.

ETIOLOGY

Optic atrophy is closely related to the fundus changes in toxoplasmosis, Tay-Sachs disease, and many other conditions. In hydrocephalus the atrophy is nearly always primary in type. Secondary atrophy is slightly commoner in cases of oxycephaly. Optic atrophy may be linked with maldevelopment of the skull, disease of the central nervous system, poisoning, febrile illnesses. Birth or postnatal injury may be incriminated. In obscure cases a likely etiology would be birth trauma.

GENERAL ANESTHESIA AS AN AID TO EXAMINATION

The author emphasizes the necessity of adequate examinations, which usually are best carried out with the patient under general anesthesia.

Comment: It is unfortunate that the paper cannot be reproduced in its entirety, as much for the delightful British witticisms in the discussion as for the further information derived. Mr. Doggart made a point of referring to the prolongation of the usual newborn babe's "blank stare" in cases of delayed myelination or of developing optic atrophy. In the discussion of the paper Mr. Lloyd took the author to task on this point, citing several members of his own family who had such a stare without optic atrophy, and further mentioned the lady who thought she was about to be accosted, or a number of people in a boat passing another group of people in a boat on the River Thames—none being a sign of optic atrophy. Mr. Doggart said that he had not meant to imply the stare as pathognomonic of optic atrophy, and after hearing of the examples of individuals in Mr. Lloyd's family, was fascinated at the notion of Mr. Lloyd and his household sitting at the end of the day in a collective catalepsy, and he hoped to hear more of Mr. Lloyd's family history at a future Congress. Would that certain of our American meetings could be similarly livened!

A point made by the author, and perhaps experienced by many of us, is the child who has no apparent vision as an infant, with borderline disks, whose parents bear him back in triumph several years later with what appears to be normal vision. As pointed out, a prognosis is difficult to give in the face of what may be slowed development, and delayed myelinization is as good an explanation as can be found.

As pointed out by Hollenhorst in the February, 1957, Survey of Ophthalmology, (1957, *2:* 39) general anesthesia is not routinely necessary for fundus examination of

small babies—and even young children, provided they are handled properly. The author of this paper leans toward general anesthesia.

It has not been my impression that optic atrophy occurs very often in hydrocephalus. The author states that it is "nearly always primary in type, and the severity does not tally with the amount of skull enlargement." My neurosurgic colleagues feel that funduscopic examination is usually negative in hydrocephalus. This seems reasonable, since the enlargement of the skull effectively limits the amount of optic nerve change due to increased pressure. However, an infant with bilateral subdural hematomas may appear much like hydrocephalus, with the shape of the head and the bulging of the fontanelle exactly the same. Facial expression is more likely to be intelligent in the subdural hematoma case, and 50 per cent of all infants harboring subdural hematomas show retinal hemorrhages.

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THE OCULAR MUSCLES

PROGNOSIS IN CASES OF STRABISMUS WITH SPECIAL REFERENCE TO ORTHOPTIC TREATMENT

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Brit. J. Ophth., 1957, *41:* 129–152

When orthoptic treatment was first practiced, it was thought that, if it were applied in cases of nonparalytic strabismus where there was good visual acuity is each eye, restoration of normal binocular function would invariably result. In 1939, when Chavasse published his theories relating to the binocular reflexes and their development, the true limitations of orthoptic treatment became more widely recognized. The important fact then emerged that the earlier the onset of a constant strabismus and the longer the interval of time before corrective treatment is carried out, the less likely it is that normal binocular function will be restored, no matter how long orthoptic treatment is continued.

Experience with a large series of cases of strabismus and the study of the work of Chavasse have convinced the authors that in certain cases binocular single vision cannot be attained whatever the treatment, while in others, provided the correct treatment is given, the restoration of binocular single vision is certain. The correct treatment varies according to the type of case; it may consist merely of appropriate spectacles (with or without the assistance of orthoptic treatment), or of surgical treatment (with or without the assistance of spectacles and orthop-

tic treatment), or of orthoptic treatment only. As a result of the indiscriminate prescription and application of orthoptic treatment in all cases of nonparalytic strabismus, many patients so treated fail to regain normal binocular function. The failure of orthoptic treatment in these patients, however, is due to the fact that it was not indicated and should not have been attempted.

After studying the history of a case of strabismus and making a thorough examination, it should be possible in most instances to decide what sort of treatment is needed and to give a fairly accurate prognosis with regard to the possibility of restoring binocular single vision. Although the prognosis in young infants too uncooperative for examination on a major amblyoscope may have to be guarded, it can still be made with a reasonable degree of accuracy.

Orthoptic treatment is unquestionably of great value in the cases in which it is justified, but the time spent in giving orthoptic treatment when it is not justified is time wasted. Consequently, great care should be used in selecting patients for orthoptic treatment, especially in the case of nonparalytic, nonaccommodative convergent strabismus. The results obtained in 213 patients with strabismus of this type have been divided into three categories: (1) restoration of binocular single vision, 24 cases (11 per cent); (2) subnormal binocular vision, with equal or nearly equal visual acuity, normal retinal correspondence, and doubtful fusion, 73 cases (35 per cent); and (3) defective binocular function, with intractable amblyopia, lack of normal retinal correspondence, abnormal retinal correspondence, and latent nystagmus, 116 cases (54 per cent). The results obtained by orthoptic treatment given to 165 of these patients (combined with operation in 138) were in harmony with those obtained in the group as a whole: (1) restoration of binocular vision, 16 cases (10 per cent); (2) subnormal binocular vision, 64 cases (39 per cent); and (3) defective binocular function, 85 cases (51 per cent). In 48 patients who had no orthoptic treatment, the results appeared to be slightly better so far as the first category was concerned: (1) restoration of binocular vision, 8 cases (17 per cent); (2) subnormal binocular vision, 9 cases (19 per cent); and (3) defective binocular function, 31 cases (64 per cent).

Although several diagnostic sessions may be needed, especially in the case of young children, an early prognosis concerning the standard the patient will probably attain in terms of binocular function should help to eliminate much unnecessary and unrewarding work and so allow more time for concentrated treatment in cases in which a successful result may be expected.

A study of the history in convergent strabismus shows that with few exceptions the results depend on the age of the patient; his age at onset of strabismus; the mode of onset, i.e., constant or intermittent; and the duration of the strabismus before the visual axes are aligned by operation or other means. Given the necessary data from the history and from clinical investigation, and with a decision in relation to the standard of binocular function the patient is likely to regain, the ophthalmologist and the orthoptist can agree to limit the treatment to the attainment of this end. Thus it should no longer be necessary to "try" orthoptic treatment. Orthoptic treatment is either indicated or not indicated. It is indicated only if there is a reasonable chance of thereby helping the patient

to acquire some form of useful binocular vision. It is not indicated if there is clearly no chance of achieving any useful form of binocular vision.

Orthoptic treatment may be valuable in all types of nonparalytic accommodative convergent strabismus. In patients with nonparalytic nonaccommodative convergent strabismus of early onset there is rarely any chance of binocular single vision except in certain instances in which the visual axes have been made approximately parallel by operation within the first 2 or 2½ years of life; when the onset is later (2 to 3 years), binocular vision of a subnormal type may develop, and in come cases be superseded by full binocular single vision, provided the visual axes have been made approximately parallel, and its attainment may be greatly helped by orthoptic treatment; and when the onset comes at 3 to 5 years or later, normal binocular single vision should develop after operation, even if the operation is postponed until later in childhood or even early adult life, provided adequate orthoptic treatment and supervision ensure equal visual acuity, absence of suppression, and other desirable qualities.

The prognosis in primary divergent strabismus is generally good even when the deviation is constant (provided there is good visual acuity in each eye), for in many cases the strabismus began in an intermittent fashion. Operation is needed in most cases, but orthoptic treatment alone is sometimes sufficient in patients with intermittent divergent strabismus. The correction of the refractive error if myopic or astigmatic and the correction of anisometropia may be of great value.

In patients with congenital paralytic strabismus, if binocular functions are good, even if binocular single vision is not demonstrable in any position of the gaze, the prognosis is good for patients who receive adequate surgical treatment. If binocular vision is absent the prognosis is usually poor unless the surgical treatment is carried out at an early age.

Comment: This is a most pertinent article. Its thesis is that orthoptics should not be a routine part in the treatment of every case of strabismus but that orthoptics should be saved for those cases that have a chance to regain normal binocular vision. The authors review the statistics of 287 cases of esotropia in which the visual axes have been rendered approximately straight by surgery, glasses or nature. Ninety-eight (34 per cent) achieved single binocular vision whereas 189 (66 per cent) did not. Further breakdown of the figures revealed that of the 98, 74 were fully or partially accommodative whereas only 24 were entirely nonaccommodative. Moreover, the average age of onset of these 24 cases was 4.8 years whereas for the failures it was under two years of age. The period between the onset of strabismus and the straightening of the visual axes was only half as long in the successes as compared to the failures. In other words, in any case of nonaccommodative esotropia it is a waste of time to give orthoptic training unless there was a late age of onset or a short interval between the onset of the esotropia and the straightening of the visual axes.

These opinions are shared by many in this country. It is for this reason that early treatment is urged to reduce the interval between the onset of strabismus and the straightening of the eyes. Moreover, in a neglected case it is useless to try orthoptic training which is almost certain to fail. As the authors state, it is not so much a failure of orthoptic training but a failure on the part of the oculist prescribing orthoptic training.

PHILIP KNAPP

NEW ORTHOPTIC TECHNIQUES

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Tr. Pacific Coast Oto-Ophth. Soc., 1956, *37:* 113–120

New orthoptic techniques depend largely upon new ophthalmologic research. Thus the new therapeutic methods to be described have been developed on the basis of experiments indicating the strength of peripheral fusion. In Burian's experiment, the peripheral stimuli, which were strong enough to break central fusion, were but vaguely perceived by the subject; their shape was not even recognizable, yet the binocularly seen central image would appear double, no matter how hard the observer tried to maintain central fusion. The importance of peripheral fusion has also been emphasized by other workers, and Keiner even calls the arousing of peripheral fusion the provisional aim of orthoptics. Only after the training of the peripheral retina can one proceed to the training of simultaneous binocular vision with the retinal center, the final aim of which is central fusion. In patients with a central sensory disturbance, such as suppression, or anomalous retinal correspondence, or diplopia, strong peripheral fusion ability may already be present, permitting extensive fusional movements. Burian maintains that only in patients who have such a sensory disturbance of the central parts of the retinas are fusional movements elicited by peripheral retinal stimuli, and that if no central disturbance exists, the patient suppresses the image of one retinal periphery.

In practice, this involves the simple principle of starting with the skill the patient already possesses and from there working gradually into the field in which his disturbance lies. Training in these patients should therefore begin in the periphery with peripheral fusion slides, or peripheral stereopsis slides. When necessary fusional amplitudes have been obtained, central suppression can then finally be eliminated with the conventional first grade slide. The process can be illustrated by reference to certain specific conditions. In children with amblyopia ex anopsia, for instance, when there is no strabismus, the eyes can be presumed to have remained straight because of some peripheral fusion hold. These children, with visual acuity in one eye as low as 20/200 and with total suppression of one central image, nevertheless have excellent recognition of stereopsis and excellent fusional amplitude, provided the targets used are large enought to avoid the central, suppressing area. In the past, the usual procedure of total occlusion of the nonamblyopic eye in these children has led, at least occasionally and perhaps often, to the onset of strabismus which required surgery for correction. When peripheral fusion is used, fusional amplitudes can be increased from the very beginning of the occlusion period. The first indication of esophoria or exophoria can be counteracted immediately with fusional amplitude in the appropriate direction in order to prevent a possible strabismus.

Secondly, in cases of eccentric fixation, when the normally fixating eye is covered, and the deviated eye takes up a definite eccentric fixation, either as the

result of a macular lesion or because the macula has been so strongly inhibited that an eccentric point is chosen for fixation, the occlusion of the good eye will have no effect in improving macular vision in the deviating eye. It has been possible, however, to establish a form of stable binocular vision in such cases by means of peripheral fusion, in spite of the low acuity of one eye. First, occlusion of the eccentrically fixating eye is carried out until the fixation of the amblyopic eye appears no longer eccentric, but merely wandering. This has taken as little as three months, and as long as one year. When it has been accomplished, orthoptic treatment is started with large steroscopic rings. As soon as some degree of fusion becomes evident, the patient is returned to the ophthalmologist for possible surgical treatment. If there has been no fusion response by the end of 12 treatments, the treatment is resumed immediately after operation.

Peripheral stereoscopic ring targets, such as those used by Swan, in which the rings appear gray or black when fused but bright red or green when seen separately, were found to be almost immediately effective in strabismus with or without normal retinal correspondence, eliciting prompt and correct stereopsis, and fusional movements when the tubes of the amblyoscope were converged and diverged from the patient's angle.

Thirdly, orthoptic treatment in anomalous retinal correspondence has in the past been prolonged, because attempts were first made to obtain simultaneous macular perception using dissimilar slides, e.g., the lion and cage on the major amblyoscope.

About 1945, Marianne Eyles and the author began to notice that patients with anomalous correspondence obtained stereopsis and fusion long before they could obtain simultaneous macular perception with dissimilar slides. Consequently, a series of slides using a peripheral fusion element in combination with central simultaneous perception elements in various sizes was devised and has consistently been found effective in shortening the time required for the establishment of normal correspondence. The fusion elements of these slides may be fused at the first trial; more often, however, they are overlapping at first and then are fused. Rapid movement of the target at varying speeds and varying amounts of sweep also help to elicit fusion. When the dissimilar targets are seen superimposed with movement, then ordinary dissimilar slides, such as the lion and the cage, are quickly substituted, because at this stage the anomalous correspondence is corrected. Finally, the movement is reduced to zero, while superimposition is maintained. Concurrently with this procedure, fusional amplitude can be developed in each direction even before the dissimilar elements are seen superimposed.

All of these methods are intended for use before or after operation. Most postoperative deviations occurring after what at first appears to be a good cosmetic result are due to absence of fusion hold, which in turn is due to uncorrected anomalous retinal correspondence, or monocular or alternating suppression. Even moderately efficient peripheral fusion hold will stabilize cases of

each of these types in the excellent postoperative position so that the remaining central disturbances can be corrected.

Finally, the treatment of patients with heterophoria, especially when convergence insufficiency is present, must be considered. Nothing but good fusional amplitude with foveal targets usually suffices to relieve the discomfort of the patients with convergence insufficiency. Yet many are unable to maintain fusion convergence for more than 10 or 15 diopters, whereas the normal is 70 or 80 diopters. This block at 10 or 15 D base out on the major amblyoscope can be overcome by presenting the patient with the large peripheral rings which employ peripheral fusion and peripheral steropsis. By following this with the peripheral and other slides, a marked increase in convergence can be secured even in one visit. The succeeding visits can then be spent in building up the full range with foveal targets, which is almost always necessary for complete relief of symptoms.

In short, the use of peripheral fusion slides and peripheral stereoscopic slides has led to the development of new orthoptic techniques producing quicker results.

Comment: The author describes the theoretical background and strength of peripheral fusion as depicted in the experiments of Burian, Winkelman, Ogle and Keiner. She then enumerates the advantageous use of peripheral fusion training in specific categories.

First, in cases of amblyopia ex anopsia without manifest strabismus, she claims that occlusion may disrupt peripheral fusion which is presumably holding the eyes straight. She therefore builds up the amplitudes of peripheral fusion to prevent the development of a manifest strabismus. This has long been a topic of debate. In my experience occlusion has not produced a manifest strabismus if the precaution of correcting fully any significant refractive error has been done before starting occlusion. On the contrary, cases with a deviation have had the amount of deviation lessened as suppression and amblyopia have been eliminated.

Secondly, in cases of fixed eccentric fixation where occlusion of the good eye is worthless, she advocates occlusion of the eccentrically fixating eye for from three to twelve months. By that time, the fixation will have ceased being fixedly eccentric but will be roving. At this point she gives peripheral fusion training and then refers the patient for surgery. We have tried this form of occlusion since Swan's description of it. In our hands it has failed uniformly, but perhaps we failed in not keeping up the occlusion for a sufficiently long time. If we had succeeded in changing the fixation form eccentric to roving, we next planned to occlude the nonamblyopic eye until the amblyopia was overcome. Then we would consider methods of straightening the eyes.

We no longer treat anomalous correspondence orthoptically so that I am unable to comment on this phase of her paper.

Fourthly, our experience agrees with hers that building up peripheral fusional amplitudes helps maintain cosmetic surgical alignments. Our follow-up has been too short to be certain whether this will be permanent but the early results are most encouraging.

I think her technique of building up convergence amplitudes with large targets before shifting to small ones an excellent one.

PHILIP KNAPP

THE ORBIT

THE CORRECTION OF EXOPHTHALMOS AND LEVATOR SPASM

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Plast. & Reconstruct. Surg., 1956, *18:* 411–426

As late as 1930, a confirmed diagnosis of malignant exophthalmos left the doctor with little hope of preventing permanently reduced vision, possible blindness, and sometimes even death. Then in 1931 Naffriger reported a case of severe exophthalmos relieved by decompression of the orbital contents into the anterior cranial fossa. His first and subsequent reports are a landmark in the understanding of the pathology underlying the condition and present a proved surgical treatment. Nevertheless, it is a formidable procedure which the patient views with alarm, and rightly so. Orbital decompression was a distinct advance toward a solution of the problem, but a simpler approach was indicated. In 1889, Kroenlein described a lateral approach to the orbit, a blind operation, which he demonstrated to be feasible for surgery of the retio-orbital space. In 1911, Dollinger reported a successful operation on a patient with a malignant exophthalmos using lateral decompression of the orbit. Tinker modified the Kroenlein incision to avoid injury to the filaments of the facial nerve, keeping within the triangular safety zone at the rim of the orbit. Then several cases were reported describing techniques for decompression into the sinuses.

TECHNIQUES OF OPERATION FOR DECOMPRESSION

The lids are sutured together, either at the time of operation or several days previously. One sided decompression seems preferable, the other side being operated on two or three weeks later. The incision begins at the posterior end of the zygomatic arch just in front of the tragus, ascends vertically for 5 cm. and then curves medially and forward to the hairline. The base of the flap should include the superficial temporal artery. The flap should be elevated from the rear to expose the strong temporal fascia along the zygoma, care being taken that all planes of tissue are lifted off the temporal fascia in a solid group, particularly anteriorly, where the malar part of the temporal fascia is covered by a dense area of fatty areolar tissue. Otherwise the nerve supply to the orbicularis oculi and frontalis muscles may be injured. The temporal fascia is cut in a crescentic manner, somewhat below and anterior to the skin incision. The temporal muscle is not separated from its bony origin and reflected downward with the fascia. The overhanging lip of the arch formed by the malar and frontal bone may be removed with bone forceps. A trephine opening is made into the lateral wall of the orbit which is formed by the zygomatic and frontal bones. Posteriorly,

the outer table of the greater wing of the sphenoid is removed with a chisel, exposing a thick cancellous layer. This is curetted out (in a manner similar to that for mastoid cells), exposing the shiny inner plate of the orbital surface of the sphenoid. This in turn is carefully curetted out. Bleeding is controlled by bone wax. Now the whole area may be enlarged downward to the upper border of the inferior orbital fissure. Care must be taken not to enter the skull through the spenoid bone or to injure the maxillary nerve at the lower part of the operative field. The size of the opening obtained is ample for decompression.

In 33 patients with progressive exophthalmos so operated, there were 7 males and 26 females, ranging from 20 to 65 years of age. Ten were under 30 years, 12 were between 30 and 40 years, and 11 were over 40. There were only 2 colored patients, the remainder being white. In these cases, decompression through the lateral wall of the orbit was performed bilaterally in 20 patients, and unilaterally in the 13 remaining. There were 55 decompression operations on 33 patients with no mortality. One case was decompressed a second time.

In a follow-up over a 3 year period, it was noted that in the cases operated upon where the exophthalmos was stationary and levator spasm was absent, the decrease in exophthalmos was more rapid and more striking than in the cases where levator spasm was a postoperative factor and active disease was present in the orbit (as expressed by edema of conjunctiva etc., at the time of surgery).

In the former cases, the average drop in exophthalmos readings was 6 mm., whereas in the latter, the average drop was under 5 mm. Where no levator spasm existed after decompression, the ocular muscles regained their tone more quickly, particularly in cases with paresis of the superior rectus muscle.

Edema and conjunctival irritation subsided more quickly where levator spasm was not present.

In cases where levator spasm was marked in only one eye, the exophthalmos was usually more pronounced on that side.

The levators were operated upon as an adjunct to the decompression in 12 cases, bilaterally in 9 cases. In 3 cases of unequal exophthalmos, only 1 eye was operated upon. In one case of unilateral exophthalmos, the levator was surgically weakened and no decompression was necessary.

Because of a residual elevation of the temporal side of the lid, the first 4 cases were re-operated upon with satisfactory results.

In all cases the levator spasm was corrected, but as the skin attachment to the levator was severed, there were noticeable resultant skin folds when the lid was opened to its normal position. In 5 cases, there was marked overcorrection with noticeable ptosis, which eventually returned to a satisfactory level in four to five weeks.

In 4 cases where muscle palsies had been a problem, there was improvement in a few months. However, some edema in 3 cases remained for several weeks. Edema was particularly noticeable in one case in which a biopsy of the lacrimal gland had been made. I believe there was leakage from the lacrimal gland, for it took 2 months to subside.

The most satisfactory results were obtained in the cases with a short history and no hard resistance to the eye.

Comment: This report of 33 cases of progressive exophthalmos that underwent a decompression operation by the lateral route represents a comparatively large series. It is unusual to see such a report by a surgeon other than those trained in the specialty fields of ophthalmology or neurosurgery. Although in the original article the author discusses many aspects of the problem of endocrine exophthalmos, this editor will confine his remarks to that portion of the paper dealing with the decompression operation and the procedure for the correction of levator spasm.

By a long incision and a large flap, the author obtains a very good exposure of the lateral wall of the orbit. It is my feeling, however, that an adequate exposure is also possible through a smaller incision, such as described in an article by Berke (Arch. Ophth., 1954, *51:* 609). In general, the final cosmetic blemish on the side of the face will be less noticeable where short incisions are used than with long curved incisions such as originally described by Krönlein and the modification described by this author.

In his description of the surgical technique, the author states that he obtains "ample" space for decompression but does not give the actual dimensions of his opening in the lateral wall of the orbit. This is an oversight common to many of the articles that have been published in the past few years on this particular approach for decompression. Unless the dimensions are stated, it is difficult to settle the question as to which approach to the orbit offers the greatest space for decompression. Although I, too, am an advocate of the lateral approach, I honestly question whether some of these "lateral orbitotomies" offer as much space for decompression as the extensive "unroofing" procedures described by some neurosurgeons.

In his discussion of the postoperative care and results of the decompression surgery, the author recommends that pressure dressings be applied for a period of 10 days after surgery. For those readers who may contemplate performing a decompression operation I would sound a note of caution as to the amount and duration of pressure to be applied to a globe whose circulation is already embarrassed by the soft tissue swelling around it. There are cases on record wherein the patient was found to be blind in one eye upon recovery from surgical anesthesia. In these cases undue pressure on the globe sometime during the course of surgery was believed to be a factor in the ensuing blindness. Furthermore, if sufficient bone from the side of the orbit is removed and the bleeding carefully controlled, the space for decompression should be adequate to handle the postoperative edema without prolonged pressure on the eye.

The author's interest in the correction of levator spasm, which so often accompanies endocrine exophthalmos, is an interesting aspect of this paper. For those readers who would be interested in the surgical details of such a correction it would be best to consult the original text.

The author uses the term "levator" in its broadest sense, to include the smooth muscle of Muller in the upper eyelid. Some anatomists would consider the smooth muscle of Muller to be a muscle separate from the levator proper by reason of its separate nerve supply and difference in the make-up of its muscle fiber bundles. In using the term levator in its broadest sense, the author also implies that the entire muscle is in spasm, whereas I believe the majority opinion is of the belief that only the spasm of the tarsal muscle of Muller accounts for the change in the position of the upper lid.

In the original text, the author gives a detailed explanation of his theory as to the role of levator spasm in the production of exophthalmos. Although the results of his decom-

pression surgery in the cases with levator spasm were not as good as in those cases without levator spasm, I do not feel that this factor completely supports the theory that the levator spasm makes the exophthalmos worse. It is my own feeling that the levator spasm accompanies the disease rather than causes it. In an attempt to prove his theory, the author operated on a case of levator spasm prior to decompression but did not find that the operation on the eyelid brought about any significant change in the exophthalmos.

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THE PUPIL

RELATIONS OF CHANGES IN PUPIL SIZE TO VISUAL DISCOMFORT

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Illuminating Eng., 1956, *51:* 537–549

An attempt is made to correlate the pupillary contraction to light flashes of various intensity with the sensation of discomfort experienced by the subject. It is thus hoped to obtain an objective measure of discomfort.

Apparatus: The subject's left eye is used for light stimulation, the right eye for photographic registration of pupillary responses.

The light stimulator is an elaborate system, containing 11 lenses, 2 light sources, a beam splitter, solenoid-controlled shutter, 2 sets of apertures and neutral grey filters. The stimulus pattern presented to the subject's eye by this device consists of (A) an "adapting stimulus" of variable brightness and constant area (51 degrees visual angle), and (B) "momentary stimuli of 1 second duration and variable rate, intensity and area (1.5 to 51 degrees visual angle). The two stimulating fields are placed concentrically. As fixation target, a pair of crosshairs intersect at the center of the stimulating fields. The exit "pupil" of the optical system measures 1.5 mm. The light entering the subject's eye is thus not influenced by the size of the pupil.

The recording system is similar to the one first described by Bellarminoff in 1885 (not mentioned by the authors). The iris is illuminated by a rectangular patch of infrared light, 5 by 11 mm., which is placed horizontally across the eye. The image, formed by two lenses, passes through a horizontal slit-mask onto infrared-sensitive 35 mm. film. This film travels at constant speed (¼ inch per second), at right angles to the direction of the slit mask. The changing pupillary diameter thus appears as a clear band of varying width on the film negative. Time of stimulation of the left eye is indicated on the film record.

Experiment: Three brightness levels of the "adaptation stimulus" were chosen to correspond approximately with values used by Luckiesh and Guth in an earlier investigation. These equivalent values are given as 71, 450 and 2258 trolands.

In the "objective" studies (5 subjects), the "adapting stimulus" was turned on for 30 seconds; then, 7 successive one-second "momentary" stimuli were given with dark intervals of 9 seconds. In successive experiments, the intensity of the "momentary" stimuli was increased from below pupillary threshold to a level beginning to cause discomfort. The pupillary contractions, registered on the film strip, were analyzed with a magnifier and scale. The initial pupillary diameter and diameter at the peak of contraction were measured, and the values for the last 5 reactions in each run were averaged.

In the "subjective" experiments (4 subjects), the subjects were asked to describe the sensations provoked by stimuli of various brightness (ranging from "no discomfort" to "intolerable").

Results: (1) The pupil did not maintain a steady diameter within the 30 seconds of "adaptation" but continued to oscillate. These fluctuations occurred about every 1 to 5 seconds and extended up to 2.5 mm.

(2) In general, an increase in stimulus intensity resulted in more extensive pupillary constriction. With the light intensity at the threshold of subjective discomfort, variations among subjects were found to range from 0.35 to 1.93 mm. contraction, with an average of 1.5 mm.

(3) At a given brightness, the extent of pupillary constriction was found to vary with the area of the stimulus.

(4) The threshold for pupillary constriction was found to be far lower than that for visual discomfort. The "threshold of involuntary blinking", i.e., the light intensity at which blinking can no longer be suppressed, was several times higher than that of discomfort.

(5) When the iris of the stimulated left eye was paralyzed by the conjunctival instillation of 6 drops of a 2 per cent solution of homatropine, no change in the threshold of glare discomfort was observed. When both eyes were treated with homatropine, the discomfort threshold—within the experimental situation—was found to be raised, even though none of the subjects were able to go out into the open and face the sky without acute discomfort.

Conclusions: (1) The authors believe that pupillary constriction has value as an index for glare discomfort. This value is limited by the variations of the pupillary response with stimulus area.

(2) The fact that the pupillary constriction which accompanies light stimulation at a given intensity varies with the area of the stimulus, is explained by the assumption that ". . . the distribution of activity among the motor units of the sphincter muscle which controls the closing of the iris varies with the distribution of light on the retina. . . "

(3) As to the origin of the glare discomfort, it is believed that the pupillary contraction is, at least in part, responsible. Contraction of the pupillary sphincter is supposed to stimulate sensory nerve endings in the fifth nerve. This stimu-

lation is believed to "contribute to the pool of excitation" which, among other effects, leads to involuntary blinking and discomfort.

(4) The decreased glare sensitivity observed under the influence of bilateral homatropinization is thought to be due to the absence of pupillary constriction. Persistence of glare discomfort in subjects with partially homatropinized eyes with only negligible pupillary constriction is explained as follows: "Since partial paralysis involves blockage of some of the myoneural junctions, the contraction would probably involve an irregular pattern of motor units. The nonuniform pull in different parts of the muscle which results from this might increase the effectiveness with which a pupil constriction would stimulate the 5th nerve endings." The intolerable discomfort experienced by subjects with fully homatropinized eyes upon facing the sky is not explained.

Comment: In this work, a great deal of thought and care have been expended on setting up a well-designed experiment. The apparatus, though not original (Bellarminoff, 1885, 1887; Braunstein, 1894; Fuchs, 1903; Piltz, 1904; van der Tweel and Bleeker, 1951), appears ingeniously constructed and could lend itself to the solution of a number of interesting problems of the type attempted. Observations like the constant spontaneous oscillations of the pupil or of the great variation of values obtained from different subjects, and the realization of the necessity of objective recording and of averaging of numerous experiments in this type of research, are valuable contributions.

It is, however, unfortunately evident that this work was not guided by thorough knowledge of the anatomy and physiology of the iris and its nervous control. Some of the conclusions are entirely unfounded. For example, nothing is known of the existence of pressure-sensitive fifth nerve endings in the iris. A causative relation between pupillary contraction and glare discomfort is unlikely (*cf.* Hopkinson, 1956). No discomfort of the kind caused by glare is experienced when the pupil is artificially contracted, for example by drugs or by diffuse light. Furthermore, the sensation of discomfort evoked by short, bright light stimuli appears instantaneously, while pupillary contraction requires a full second or even longer to reach a substantial degree.

The reported raising of the discomfort threshold for artificial glare as result of bilateral homatropinization may be subject to doubt and the possibility of experimental error would have to be excluded. The authors do not deny the existence of hypersensitivity to bright daylight in subjects with atropinized eyes; they do not, however, explain why daylight and bright artificial light should produce opposite effects.

The authors' explanation of the glare discomfort experienced by subjects with partly homatropinized eyes is equally unconvincing, because there is no reason to suppose that some fibers of a muscle as thin as the iris sphincter should remain unaffected while others are paralyzed, when the entire organ is flooded by homatropine. Unequal pull in different portions of the iris, as assumed by the authors, would lead to distortion of the pupil, which is not observed during the period of recovery from homatropinization.

OTTO LOWENSTEIN

GLARE DISCOMFORT AND PUPILLARY DIAMETER

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J. Optical Soc. Am. 1956, *46:* 649–656

It has been suggested that pupillary contraction could be used as an objective measure of glare discomfort. Limited experiments were undertaken to re-investigate the problem.

Method: In a small room with white walls of uniform reflection, the level of luminance could be varied. The subject fixed on a point at eye-level on the opposite wall, at 10 foot distance. As glare source, a 150 Watt reflector spot light was placed 10 degrees vertically above the fixation point. The wall behind the subject was painted dull so that changes in brightness of the glare source (up to 20,000 footlambert) had little effect on room illumination.

For observation of the pupils, the enlarged image of the subject's eye was projected and the pupillary diameter measured with a scale graticule. Photographs were taken with an Argiflex camera on fast panchromatic film; in experiments requiring dim light, a photographic flash was used to expose the picture. After each flash, 5 minutes of rest were allowed.

Using 2 subjects, 6 experiments were undertaken. The value of the "surround brightness" was chosen at 0.16, 0.66, 1.0, 48, 55 and 130 footlambert. In each experiment, the subject's eye was successively adapted for 5 minutes to glare-light intensities rated as "just perceptible," "just acceptable," "just uncomfortable," "just intolerable," and "definitely intolerable." Measurements and records were taken for all conditions.

Results and conclusions: No direct relation was found between pupillary diameter and the sensation of glare discomfort. Other factors, especially the total illumination received at the eye, appeared to govern the pupil. Thus, for a given brightness of the glare source, the brighter the surroundings the smaller the pupil, even though the sensation of glare *diminished* with an increase of background brightness. In contrast, for a given brightness of the environment, the brighter the glare source the smaller the pupil, but in this case the glare *increased* as the pupil contracted.

A small bright spot surrounded by dark background created a strong sensation of glare which could be relieved by "contrast grading," i.e., by introducing an area of intermediate brightness between the glare source and the dark surrounding. The pupil, however, was not affected by contrast grading. On the other hand, the pupil could be contracted by diffuse light without discomfort.

The author observed continuous pupillary oscillations when the eye was exposed to a glare source. Similar oscillations were seen when the subject was asked to fix hard on the fixation point for some time. The mechanism of these oscillations is discussed. The question is left open whether they originate from psycho-sensory stimuli, evoked by the sensation of discomfort, or whether they

might be due to a condition of disbalance between pupillo-constrictor and pupillo-dilator influences in the iris, caused by the diversity of the retinal illumination at different points of the field. This "disbalance" may be, in part, a cause for discomfort.

Comment: The experiments cited appear to prove convincingly that no direct relation exists between pupillary contraction and the sensation of glare, and that therefore, pupillary contraction cannot be used as an index of glare discomfort. We would question the author's suggestion that an unstable condition *in the iris*, brought about by uneven illumination of the retina, could be a source of glare discomfort (*cf.* Fugate and Fry, 1956). Pupillary oscillations similar to the ones observed by the author under the condition of glare are evoked by uniform illumination of the entire retina, even without the sensation of glare. Since these movements are more easily discernible in a brightly illuminated eye, they are generally believed to be more pronounced in very bright light, but when the movements are recorded, it can be seen that this is not always the case.

OTTO LOWENSTEIN

THE RETINA

FIELD OF VISION AND DARK ADAPTATION IN PATIENTS WITH SENILE DEGENERATION OF THE PIGMENT EPITHELIUM OF THE RETINA

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Arch. f. Ophth., 1957, *158:* 326–333

Field of vision and dark adaptation were studied in three men and one woman between the ages of 52 and 74 years. The field of vision was examined with the aid of Maggiore's perimeter on three successive days or the perception of white, red, blue, green and yellow colors. A dark adaptometer of Goldmann-Weekers' type was used for the study of dark adaptation. Examination of the fundus in the area of the equator revealed senile pigmentation of the outer layers of the retina, with pigment figures similar to bone corpuscles in addition to pigmented granules and fragments. (There was no migration of pigment into the inner layers of the retina.) These senile changes in the pigment epithelium were pronounced in three of the four patients and were moderate in one. The limits of the field of vision for the perception of white were normal in all four patients. The field for the perception of red and blue showed a marked inversion in the three patients with pronounced changes of the pigment epithelium, and the field for the perception of yellow showed a concentric narrowing in two of these three patients. The inversion was not complete in one patient

with moderate changes in the pigment epithelium; there was only an overlapping of red and blue, and the narrowing with respect to yellow was moderate. Dark adaptation showed a normal course in all four patients.

Progressive disturbance of blue and yellow sensitivity in patients with senile pigmentation of the retina suggests the presence of special elements in the retina which transmit the perception of blue-yellow. The fact that the light sensitivity was not reduced in these patients with senile pigmentation of the retina seems to confirm the observation by other workers that light sense is not disturbed in patients of advanced age, provided their eyes are normal also in other respects. Tests of light sense under conditions of dark adaptation may, therefore, be an aid in differential diagnosis of senile degeneration of the pigment epithelium of the retina and genuine retinitis pigmentosa senilis. The latter is always associated with a reduction of the light sense under conditions of dark adaptation and the test of light sense under these conditions may confirm the clinical diagnosis in doubtful cases.

Comment: This communication from the first Vienna Eye Clinic supplements Pillat's interesting work on senile pigmentation of the retina (Arch. f. Ophth. 1950, *150:* 1).

It is noteworthy that also in this type of pigmentation, which is confined entirely to the outer avascular layers of the retina, "bone corpuscle" shape of these deposits is not infrequently encountered, suggesting that this arrangement does not have to follow vascular (capillary) channels.

Pillat suggests migration along fibers of Mueller's cells which even normally form "fibre basquets" around the percipient retinal elements. Whenever they proliferate, possibly simultaneously with the microglia in response to a demand for phagocytes (Friedenwald and Chan, Arch. Ophth. *8:* 73, 1932) the fiber network becomes even denser and migration of pigment laden phagocytes between this fibrillary meshwork could produce multiform patterns.

There is also the possibility of proliferation and metaplasia of the pigment epithelium itself, which is often seen to form multiple layers of elongated, fibroblast-like cells or glial cells in places where the first retinal neuron has perished (Klien, Am. J. Ophth. *38:* 470, 1954). Pigment deposits within such plates could also produce variable branching patterns which remain behind the vascular layers of the retina.

One might speculate even further, remembering Michaelson's unknown tissue factor *X* in areas of relative retinal anoxia (Michaelson, "Retinal Circulation in Man and Animals," Charles C Thomas, Springfield, Illinois, 1954). In the embryonic retina this factor is thought to regulate the development of the retinal vascular trees after definite patterns. Michaelson believes that this faculty to respond to relative anoxia with new formation of capillaries is not lost but becomes dormant in the adult retina and that it may be awakened again by a variety of conditions which produce mild degrees of chronic anoxia. Recently this concept has been broadened and applied to several vascular diseases of the retina such as Coats's disease, diabetic retinopathy and circinate retinopathy (Wise, Tr. Am. Ophth. Soc., 1956, also Wise, Houston, Havener, Interim Meeting Pan-Am. Congress of Ophth., April, 1957).

If, as appears likely, this senile degeneration develops secondary to choroidal vascular disease, stimulation of capillary growth outward into the avascular relatively anoxic retinal layers would not be too surprising. The endothelial and adventitial cells of such new vessels would phagocytose pigment and give it the well known pattern. For the periph-

eral senile pigmentary degeneration such neovascularization awaits histologic demonstration; in macular lesions of vascular origin such neovascularization has been demonstrated (Klein, Am. J. Ophth., *34:* 1279, 1951).

It must be conceded, however, that such response, especially in older people, may be precipitated more easily in the macular region which has three capillary layers than in the the equatorial retina which contains only one.

BERTHA A. KLIEN, M.D.

PLANNED TREATMENT OF RETINAL DETACHMENTS

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Tr. Ophth. Soc. U. Kingdom, 1956, *76:* 259–266

The most satisfactorily treated retinal detachments are those in which all the holes are found and sealed. Most of the work in curing a retinal detachment is done before the patient goes near the operating room. The first essentials, therefore, are a complete examination of both fundi and the drawing of an accurate map by the surgeon who is to operate. This map should show the principal vessels, so that the features and holes noted on it can be found later at operation and so that the best treatment can be planned beforehand for replacing the retina and sealing off any holes and thin areas in it. Binocular indirect opthalmoscopy is the best method of fundus examination in these cases, partly because it is less tiring for the surgeon and the patient than direct ophthalmoscopy.

A careful history must be taken, with special reference to the presence and direction of flashes of light and the time of onset of increased floating opacities in the vision. The sudden increase of floaters often marks the initial onset of the detachment. The site of light flashes lies most frequently diametrically opposite the position of some of the holes.

The visual acuity is determined and the refraction measured. Homatropine with cocaine and phenylephrine (10 per cent) is then instilled and half an hour is allowed to elapse. As the examination often lasts an hour and a half, both patient and surgeon must be comfortable. The patient lies on a couch with a 4-inch foam rubber mattress and a small pillow, the height of the pillow being 3 feet from the ground. The fundus examination is made with a binocular indirect ophthalmoscope using a plus 20 D aplanatic lens. After a preliminary survey the main vessels are drawn on the map and thereafter the limits and contours of the detachment. The main holes and tears can then be charted accurately in relation to vessels and meridians, and degenerate and pigmented areas can be identified. In the degenerate retina a special search must be made for thin areas

and perforations. Finally, some drops of pantocain 1 per cent are instilled into the conjunctival sac, and the periphery of the retina up to the ora serrata is examined. This is done by indenting the sclera and so causing the retina to come into the field of vision.

If the examination is made in this way for each eye, it will minimize the need for a second operation to seal primary holes, which are best treated at the first operation. It will also enable thin areas and even open holes and early detachments to be diagnosed and given early treatment in the opposite eye, especially in highly myopic patients. It is no longer enough to examine retinal detachments by direct ophthalmoscopy alone when about one-sixth of the retina, where it is thinnest, cannot be viewed by this method. When the drawing has been completed, the patient is placed in bed with double pads to enable the retina to settle back against the wall of the globe by gravity. This settling takes place gradually over several days. If the retina does not flatten with posture, however, and no retinal holes can be found to account for it, a diathermy puncture should be performed to evacuate the subretinal fluid. This will bring into view the peripheral retina, which was obscured by ballooning. It must be remembered that a diathermy electrode may plug its own hole by the coagulum attached to its tip on withdrawal, unless it is reintroduced cold to clear the way. If the diathermy puncture produces little subretinal fluid, then the nature of the detachment may be solid or complicated by vitreous retinal adhesion and vitreous retraction.

The various current operations devised to seal the holes of retinal detachments or to isolate them fall into two broad groups: those that produce a burn reaction of the deep layer of the retina and choroid, and those that produce a ridge of the sclera as well. Surface diathermy, either under indirect observation or by pilot application, is best suited to a simple hole or an isolated group of holes in a retina that has no other thin areas. Whether the application is made with a smooth end, a spiked end, or a pin, the same principle applies. Lamellar sclerectomy gives a long area of reaction and will provide a means of holding an area of retina with several holes in it or holes with adjacent thin retina. The globe shortening effect appears to be far less important than the broad grip that it gives to thin retina. The sclerectomy must be placed to cover the holes or to isolate them to the periphery. If it cannot cover the holes, then surface diathermy must be applied to the holes before the sclerectomy. An alternative procedure is the injection of 1.5 per cent caustic potash into the subchoroidal space in the area of the holes after the sclerectomy. This requires great skill and judgment, but is very effective. Giant holes must be judged individually. Many are beyond repair; some may by cured be carefully placed surface diathermy to the area of the hole, including a little of the adjacent retina to hold it; and others may need a radially placed scleral reefing, lamellar sclerectomy, or either of these combined with a plumb of solid or tubular material, such as polyethylene or supramid.

After the main operation to produce the sticky patch of choroidoretinal exudate, the subretinal fluid is let out by scleral puncture. This is often satisfactory, allowing the retina to fall back against the wall of the globe. Sometimes,

however, the subretinal fluid seems reluctant to flow. Strong suction in such cases is dangerous; it may force formed vitreous out and lead to the formation of secondary holes; and it may also carry the retina with the current passing through the hole, so that the retina plugs the hole prematurely and becomes tented at that point. Light pressure on the globe seems preferable to suction or, where there is much retinal ballooning, the injection of air or saline into the vitreous. If saline is used, the final position of the retina may be inspected, but care must be taken not to induce too high an intraocular pressure.

Subclinical or early detachments may be present in patients, especially those with myopia, who have few or no symptoms but who are found on full mydriasis to have open holes, tears, or a local detachment. If the lesions are superior, they must be treated and many operators will use surface diathermy for this purpose. A new method of treating these cases is by "light coagulation" through the media of the eye. It involves the use of a special apparatus to produce the strong light, but no surgical procedure is needed. This method is well suited for posterior holes, holes in retinas that flatten well with posture, open holes, and thin areas in the opposite eye.

In the discussion of this paper, one of the speakers emphasized the difficulties connected with deciding whether or not to operate on what looked like a possible hole in an eye with no symptoms and a flat retina. Some of the holes that looked open were really sealed off and possibly did not need any treatment. The patients should be told to report to the ophthalmologist at the first indication of floaters or flashes of light. Very often these patients go for years with a small apparently open hole remaining unchanged. Treatment, if any, might consist of mild surface diathermy around the area.

Comment: This article focuses our attention on the necessity for a careful preoperative examination of the patient. I do not know many ophthalmologists, however, who evacuate subretinal fluid as a diagnostic procedure to expose peripheral breaks. If a large amount of subretinal fluid is obtained, the eyeball usually becomes so soft that the ophthalmoscopic examination is difficult.

As in most papers published in the Tr. Ophth. Soc. U. Kingdom, the discussion that follows the presentation is very worthwhile. Sjögren stated he did not favor a buckling procedure with the implantation of foreign material. Crick suggested the use of a fine hook to pull the edge of the retina back when there was a large fold or disinsertion of the retina. Stallard pointed out that prophylactic diathermy on a small hole without detachment might lead to massive vitreous contracture with a complete detachment.

P. Robb McDonald

PROPHYLACTIC TREATMENT OF RETINAL DETACHMENT BY LIGHT COAGULATION

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Tr. Ophth. Soc. U. Kingdom, 1956, *76:* 739–750

The most suitable cases for treatment by light coagulation are early retinal detachments, prophylactic treatment of degenerative areas, and detachment caused by tumors and inflammatory diseases. Experience has proved that only light sources, whose intensity and spectral distribution are comparable to the sun, are suitable for clinical use. The apparatus used includes a special arc lamp developed by the author. The image of this lamp is formed by a lens system in a diaphragm, from this aerial image a second image is formed on the fundus of the patient by the "eyepiece" and a mirror. The image on the fundus is observed through a hole in the mirror 0.75 mm in diameter. The size of the diaphragm can be varied in order to produce coagulations of different sizes. The largest possible coagulation covers an area of half a disk diameter. Errors of refraction in the patient's eye of more than 5 diopters are corrected by a contact lens. Observations of the fundus are made with subdued light obtained by using a shutter, which transmits only 2 per cent of the light. When the full intensity of the light is desired, the shutter can be released by the observer.

The mirror is brought as close to the patient's eye as possible. Then, after the subdued light has been focused on the retinal lesion, the area is exposed to the full intensity of the light by releasing the shutter, and the development of a coagulation is seen as a whitish discoloration of the retina. Coagulation in the periphery of the fundus requires an exposure time of one second, while one-fifth of a second is sufficient for coagulations at the posterior pole.

Intensity, duration, and wave length of the radiation were so chosen that any undesired damage is impossible, provided that the treatment is properly applied.

Light coagulation leads to almost the same opthalmoscopic picture as does diathermy coagulation, except for a more subtle pigmentation during the healing process. The histologic picture, however, is different, since only the inner layers of the sclera show signs of coagulation. The vitreous and its limiting membrane are not affected. The adhesion produced by light coagulation is not less firm than that produced by diathermy. It is essential for the effect of light coagulation, that there should be a light-absorbing tissue immediately behind the retina which normally is provided by the pigment epithelium and the choroid. Highly detached retina does not absorb enough light to become coagulated. To achieve a chorioretinal adhesion, the distance between the retina and choroid must not be more than about 1 or 2 diopters.

The author summarizes 305 cases treated with light coagulation: 58, macular holes; 92, eyes with holes in the periphery (including 26 cases with an extended

detachment that had been reattached by immobilization and binocular bandage before light coagulation was applied; 72, eyes with degenerative areas without visible holes; 37, cases of postoperative treatment by light coagulation, including 18 cases of perforating injuries; 11, cases of barraging of circumscribed detachments; 18, cases of repeated vitreous hemorrhages and retinitis proliferans; 17, eyes with tumors (melanosarcomas, angiomatosis retinae, retinoblastomas, one case of Coats's disease). Twenty cases were not successful. Out of these 20 cases, 11 could be cured by diathermy operation. In the first three groups only three cases were not successful. No severe complications, such as vitreous hemorrhage, were encountered.

The special advantages of light coagulation in the field of prophylactic treatment lie in the following facts: It can be performed easily and quickly; it permits exact localization; it can be repeated as often as desired; it results in only an almost imperceptible trauma to the eye.

If, however, an extended detachment has once developed, light coagulation is possible in only 10 to 20 per cent of the cases. Therefore, the classical method of diathermy operation can not be replaced entirely by this method.

Comment: This is a most interesting paper and should stimulate some ophthalmologists in this country to evaluate this method of treatment. The fundus photographs certainly show the desired amount of reaction necessary to close the breaks in preclinical detachments, macular holes, and those areas of peripheral degeneration seen so frequently in a patient with a large detachment in one eye, or in one who has already lost an eye with retinal detachment.

The experimental work has probably shown that there is no damage to the cornea or lens. Light is reflected, transmitted or absorbed. To create its effect it must be absorbed, so it is understandable that the choroid and the retina must be in close approximation for the desired reaction to take place.

However, like any method of treatment, it is probably not innocuous and, in inexperienced hands, it would be best to try it first on animals or on eyes prior to enucleation for melanoma. This would appear to be a definite contribution to the treatment of certain types of retinal detachment.

P. Robb McDonald

HEREDITARY DISEASE

OCULAR ALBINISM WITH CHANGES TYPICAL OF CARRIERS

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Brit. J. Ophth., 1956, *40:* 721–729

Ocular albinism is a form of incomplete albinism in which the lack of pigment is chiefly confined to the eyes. The condition is relatively rare, but since it was described for the first time by Nettleship (Trans. Ophth. Soc. U. K., 1909, *29:* 123) it has occasionally been demonstrated in various families. Nettleship was aware that the disease producing gene was sex-linked, but assumed it to be recessive; recent investigations have since proved that the sex-linked gene of the condition is intermediate in its expression.

The ocular symptoms encountered in males with ocular albinism are also well known in generalized albinism. Affected individuals suffer from impaired vision and undulatory nystagmus; the retinas are poor in pigment; the choroidal vessels are seen with great clearness, and the macular areas are hypoplastic, lacking the yellow color normally seen in red-free light. The irides are bright and translucent, so that the pupils may appear faintly red. Strabismus and astigmatism are usually present. In addition, head nodding is often seen in early childhood.

Attention has been focused particularly on this complex of characteristic symptoms in males, whereas little interest has been taken in the apparently unaffected females.

However, Waardenburg (Ned. T. Geneesk 1947, *91:* 1863) was able to show, by the translucence of their irides, that these heterozygous females were carriers. A few years later, Falls (Am. J. Ophth. 1951, *34:* 41) established what had been rendered likely by Waardenburg's observation, *viz.* that ocular albinism has an intermediate sex-linked mode of inheritance; he described a peculiar ophthalmoscopic picture which he had observed in all female carriers in two American families in which male members exhibited ocular albinism.

Ophthalmoscopically, the fundus of such a heterozygous female reveals normal pigmentation in the central area. The macula has retained its reflexes, but it is often denser and coarser in its pigmentation than normal. Peripherally, a peculiar polymorphous pattern of grayish-brown, irregular patches of granular pigmentation is seen. They begin centrally as faint granules, occasionally deposited as small rings; towards the periphery they increase in size, become more confluent, and maplike, with mainly radial orientation, and are separated by areas poor in pigment with clearly visible choroidal vessels.

A family consisting of 169 members, eight men of whom suffered from ocular albinism, was studied. A total of five generations is represented. Fundus changes

characteristic of carriers were seen in fourteen females of the family. The ophthalmoscopic picture observed in the fourteen carriers was characteristic and easily recognizable, but varied with regard to the intensity of the pigmented patches and the relation between the areas with heavy and sparse pigmentation.

Other findings of interest were revealed in these carriers. One mother and her daughter had a periodic, fine undulatory nystagmus, rarely present in the darker mother but frequently seen in her blonde daughter. Another blonde heterozygous woman had a similar nystagmus. This woman suffered from visual impairment in both eyes (20/40), fairly pronounced nystagmus, and slight convergent strabismus. Her darker sister had astigmatism of almost the same intensity, a similar strabismus, but a visual acuity of 20/30 in both eyes and no nystagmus. Astigmatism and strabismus were also present in other carriers; in one case together, in the others isolated.

Of eleven carriers studied for translucency of the irides, nine exhibited the symptom, but it was absent in two dark-haired women. These findings show that female carriers may exhibit abortive symptoms of ocular albinism other than the ophthalmoscopic changes, which are constantly present, and the translucence of the irides, which is usually but not invariably present. The investigation also shows that there must be a considerable variation in the expressivity of the intermediate gene. Previous investigations may be interpreted in the same direction.

When, in the literature on this disorder, information is given as to the general pigmentation of the affected males, these individuals are usually described as blonde or white-haired, with a fair complexion. This suggests that the responsible gene has a wider effect and may produce mild manifestations of generalized albinism. In the family studied this information was available as to the general pigmentation in seven out of eight males. Of these, six were blonde, and in childhood they had had almost white hair and had not reacted to sunburn. The pigmentation increased with age; although they remained blonde in adult life, they were not strikingly fair, and they were able to be tanned by the sun to some extent. One of the deceased males with unquestionable impairment of vision and nystagmus was dark and was the son of very dark parents. This variation should presumably also be seen against the background of the expressivity of the gene.

The general pigmentation varied within wide limits in the carriers. On the whole, most abortive symptoms were present in the blondes and seemed often most pronounced in them, though those with dark hair were also sometimes considerably affected. It is reasonable to assume that the gene is also able to exert a certain, although weak, influence on the general pigmentation in carriers.

Finally, it should be noted that two female carriers and a man with ocular albinism also had cutaneous areas of depigmentation and one woman had heterochromia. That these changes should be due to the same gene as that responsible for the ocular affection is, however, unlikely, since a healthy son of an affected man also showed an area of sparse cutaneous pigmentation and a woman who was not a carrier had a lock of white hair.

The conclusion must be that the sex-linked intermediate gene which is re-

sponsible for ocular albinism varies considerably in expressivity, and has a weak influence on the general pigmentation as well as its principal effect on the eyes.

Comment: The more one learns about a subject, even such as albinism, the more complicated and intricate its subtle variations become. The form of ocular albinism exhibiting intermediate sex-linked inheritance described by the author is not a rare entity. We have well over five such families in our pedigree files at the Heredity Clinic of the University of Michigan.

As expected of any gene determined trait, and for that matter of any disease entity, considerable variability of expression exists. This is true of Ohrt's heterozygous females. Actually this should be anticipated since the gene for the trait exerts its influence in a different genotype in every affected individual. The influence of the surrounding gene milieu could hardly not be expected to influence the specific gene since theoretically no one gene ever acts alone. Subtle differences in the genotype (genetic make up of the individual) would be expected to effect minor variations in the expression of the trait. The female carriers may thus approach closely the male picture of the disease and even as in one affected male, I have seen, the reverse may occur.

Most of the affected males, at least in my families, during the first year of life exhibit most of the features of generalized albinism, namely: (1) nystagmus, (2) head nodding, (3) diaphanous irides, (4) photophobia and (5) marked blondness of hair and skin but which, with advancing age, mostly disappears or becomes modified towards the normal. Is this then a temporal albinism: A deficiency in substrate, tyrosine, enzyme or any of the numerous essential factors necessary for melanin pigment formation which exists for only a short time in the life span of the individual but which seriously influences the developing macular area, especially in the male and occasional heterozygous female? Retinal pigment is essential to the development of the retina. It must be even more necessary to assure the development of efficient macular physiology and lacking at a critical stage of development, when most needed, leads to functional aberrations.

When the ophthalmologist encounters a male exhibiting unexplained visual acuity reduction and especially when associated with nystagmus and albinoid fundus the simple experience of scleral transillumination to reveal the diaphanous iris or merely looking for the heterozygous female retinal picture in his mother will establish the correct diagnosis—ocular albinism.

HAROLD F. FALLS

THE OCULAR MANIFESTATIONS OF THE STURGE-WEBER SYNDROME

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South. M. J., 1957, *50:* 82–89

The Sturge-Weber syndrome, or encephalotrigeminal angiomatosis, is the combination of a hemangioma of the skin, usually over the area of distribution of one or more branches of the fifth cranial nerve (nevus flammeus), glaucoma, and angiomatous changes in the vessels of the meninges of the brain. Nevus flammeus may be associated with glaucoma without meningeal involvement, or with a meningeal angioma without glaucoma. The incomplete forms are more frequent than the complete syndrome. When present, the facial lesion and the glaucoma almost always occur on the same side. Nevus flammeus is usually unilateral but may be bilateral, and, when associated with glaucoma, involves the lids or conjunctiva. Glaucoma is either buphthalmic or the chronic simple type.

The ocular findings associated with nevus flammeus are dilated conjunctival vessels, vascular nevus of the conjunctiva and the episclera, peripheral anterior synechiae, heterochromia iridis, dense stroma of the iris, dilated vessels of the iris, varicose vessels of the iris, hemangioma of the iris, tortuous retinal vessels, varicosities of the retinal veins, dark red fundus, changes in the pigment epithelium of the retina, retinal detachment, dilated and tortuous choroidal vessels, hemangioma of the choroid, and cavernous atrophy of the optic nerve. The commonest intraocular vascular change is a hemangioma of the choroid.

Choroidal hemangiomas often occur as isolated lesions and are considered by Berliner to be variants of the Sturge-Weber syndrome. They present a difficult diagnostic problem when seen clinically and are usually mistaken for malignant melanomas.

The neurologic symptoms, which are due to intracranial hemorrhage from the abnormal vessels of a diffuse meningeal hemangioma, have been listed as localized and generalized epileptiform seizures, hemiplegia, hemianopsia, mental deficiency, contralateral homonymous hemianopsia, and epilepsy.

The records of six patients with partial or complete Sturge-Weber syndrome showed that nevus flammeus, which was present in four cases, was associated in one with buphthalmus; in another, with glaucoma resembling chronic simple glaucoma; in another, with an ophthalmoscopically visible hemangioma of the choroid and a radiographically demonstrable meningeal lesion; and in the fourth, with heterochromia. Glaucoma was found in four of the cases, but in none could it be directly attributed to a vascular anomaly of the uvea. In two of these cases, the glaucoma appeared to be due to secondary changes following

long-standing retinal detachment with blockage of the filtration angle. In the two patients observed clinically with glaucoma, the filtration angle was open in each, but a vascular lesion was not seen in either. However, if a fundal lesion seen in one of the six patients was a hemangioma of the choroid, it would not be difficult to overlook a similar but smaller lesion on ophthalmologic examination. None of the patients presented neurologic symptoms.

The acute rise in the intraocular pressure that takes place in an eye containing a hemangioma of the choroid when the jugular veins are compressed indicates that disorganization of the fluid traffic of the uvea plays an important part in the production of the glaucoma. Blockage of the vortex veins, with a sudden increase in the bulk of the choroid and of the hemangioma, seems to be the essential factor in the rise of pressure. Jugular compression is, therefore, suggested as a possible diagnostic aid in differentiating hemangiomas of the choroid from malignant melanomas, especially in young adults. The choroidal lesion in one of these cases had no characteristics that would have facilitated its clinical recognition, but the response to jugular compression was invariable.

Comment: Dr. Stokes has called our attention to a valuable diagnostic procedure to aid in the diagnosis of intraocular angioma which, as he correctly indicated, frequently may resemble a melanoma. *Jugular compression* is a simple expediency which, if it provokes an acute rise in intraocular pressure, is most suggestive of intraocular angioma, usually of the choroid. I should like in addition to suggest electrophoretic and protein analysis of the aqueous which, if exhibiting elevated protein content, will also be very suggestive of the presence of choroidal or retinal angioma.

A knowledge of the essential widespread signs and symptomatology of the Sturge-Weber syndrome may also aid in the differential diagnosis of intraocular lesions. This syndrome, one of the mucocutaneous group, may include typical nevus flammeus, angioma of the meninges and brain, contralateral Jacksonian seizures, intracranial calcification, heterochromia of the iris, mental aberration, hydrophthalmos, chronic glaucoma, angioma of choroid, retina, cerebellum, spinal cord and so forth. It is most important to know, as emphasized by the author, that the entity may exhibit only one or two of the above-mentioned features. In fact, this variability of expression is rather characteristic of this dominantly inherited trait. Recognition of features of the syndrome among relatives of the patient being studied might well suggest that the intraocular lesion is possibly an angioma and the only evidence of the disease.

HAROLD F. FALLS

GENERAL OPHTHALMOLOGY

UNILATERAL BLINDNESS FOLLOWING INHALATION ANESTHESIA

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German M. Monthly, 1956, *1:* 142–143

A few reports have been published on the occasional occurrence of unilateral or bilateral blindness following major surgical operations. This has been thought to be caused either by extensive blood loss or, more rarely, by an embolism to the central retinal artery. This case report of an occlusion of the central retinal artery after a gynecologic operation may show there is another cause.

A total hysterectomy was performed on a 48-year-old patient. Her history was negative for previous eye disease. Premedication was Largactil (chlorpromazine), and nitrous oxide and ether anesthesia was given through a closed system. There was no evidence of vascular disease. The blood pressure was normal during the 2-hour operation and blood loss was made up concurrently by intravenous transfusion of whole blood.

The patient complained of blindness of the left eye one day postoperatively. Ophthalmoscopic examination showed the typical picture of occlusion of the central retinal artery. The right eye was normal.

At first, no satisfactory explanation of the etiology of the arterial occlusion could be found. An interesting point, however, was noted by a physician who had witnessed the operation. He recalled that during the procedure the anesthesia mask had become displaced towards the forehead and the tubing from the mask had exerted some pressure upon the left eye.

The findings in five reported cases of permanent unilateral blindness after inhalation anesthesia resemble the above case. It is particularly significant that in all these cases the tubing of the apparatus was on the affected side. Unilateral blindness after anesthesia in eight neurosurgical cases has been reported. Pressure on the eyes from a head-rest supporting the face is believed to have been the cause. The author believes that an important causative factor in the occlusion of the central artery is faulty positioning of the anesthesia mask. By pressing on the eye ball, the mask increases the intraocular pressure in the subsequently blind eye.

Constant control of the face mask's position is necessary to avoid this accident. If a patient complains of visual disturbance postoperatively, the eyes should be examined at once. Only immediate treatment of the arterial occlusion may prevent blindness.

Comment: This case report brings to mind the article by Givner and Jaffe on "Occlusion of the Central Retinal Artery Following Anesthesia" (Arch. Ophth., 1950, *43:* 197). Due

to the paucity of reports in the literature of complications of this type, one might believe they are rare. It is possible that, human nature being what it is, complications such as this occur much more frequently but are not reported due to lack of enthusiasm on the part of physicians to discuss their mistakes. Recently, however, there have been several articles in the American and English literature implicating a mask with tight head harness in the production of postanesthetic cephalalgia. Case reports of facial nerve paralysis due to strong pressure applied to the lower jaw during general anesthesia have also been reported recently. These embarrassing and, in the abstracted case, disastrous complications emphasize again that there is an art to the specialty that we practice. Sir Robert MacIntosh, in his Jenny Hartman Memorial Lecture, published in *Anaesthesia*, October, 1956, makes many provocative statements. He does, however, bring up a point which would be well taken by all anesthetists when he says, "Should I have to be operated on, I trust my anesthetist will treat me not as an interesting case, but as a worried patient. I hope he will be the sort of man who puts art before science and on a very earthy plane and is not above taking interest in . . . small things." Attention to small details will prevent these complications. The anesthesiologist must always keep in mind the possibility of these complications. A report such as the above is worthwhile and helps to refocus our attention on the small details of our art.

PAUL DUMKE
Survey of Anesthesiology

OPHTHALMOLOGIC ASPECTS OF DRIVER LICENSING AND REPEAT OFFENSES

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J. A. M. A., 1957, *163:* 227–228

There are at present no definitive statistics as to the importance of visual dysfunctions as causes of highway accidents, in spite of the fact that driving one of the modern high-speed automobiles calls for a high degree of visual skill. The confusion that prevails in regard to this aspect of driver competency is clearly reflected in the visual standard requirements for the issuance of driver's licenses in the various states and territories. For example, the minimal visual requirements for an unrestricted license are a visual acuity, without correction, of 20/30 in 4 states, 20/40 in 32 states, 20/50 in 7 states, 20/60 in 1 state, and 20/70 in 3 states. In one state there are no visual requirements whatsoever. Only 18 states require a licensee to have adequate depth perception, and only 9 states make any effort to determine the applicant's visual-field status. Requirements for restricted licenses, i.e., for one-eyed drivers and those with subnormal acuity, are even more variable.

The first step that should be taken to rectify this deplorable situation is the setting up of a board of ophthalmologists with members chosen from the prin-

cipal ophthalmologic associations. This board should determine the standards, not only of visual acuity needed by drivers, but of other visual functions as well, and it should then endeavor to interest each state in adopting these standards. The board could also make use of data already available, working with the various state departments of motor vehicles in setting up, carrying out, and interpreting studies designed to provide more definitive data to be used in the revision of existing standards.

A few states have recently taken a great step forward in the screening of driver candidates by employing one of the various screening devices that quickly screen a candidate for visual acuity, depth perception, color discrimination, sign reading ability, muscle balance for near and distant sight, and visual fields. All of these factors must be taken into account if a person's visual skill for driving is to be accurately evaluated. Persons disqualified by such screening are referred to a physician for medical attention and for correction of defects. Those whose visual defects can be and are corrected medically may then be given their driver's licenses. Examinations of this kind have also led to the early detection of pathologic conditions of the eyes and have resulted in the saving of sight.

Repeat offenders, or drivers who have several accidents, should also be retested by a screening device and those found to have visual defects should immediately be referred to a state evaluation board for more complete study and evaluation. Boards of this sort should have more elaborate facilities for the study of visual function than those available in the screening centers. Color discrimination, depth perception, dark adaptation, reaction to glare, acuity of central and peripheral fields, and visual reaction time should be thoroughly investigated. Persons with visual defects that cannot be reasonably corrected must be prohibited from driving by the withdrawal of their licenses, or they should be allowed to drive only under definite restrictions.

Fortunately, although motor car manufacturers have hitherto been somewhat remiss in their consideration of optical problems, they are now becoming safety-conscious, and it is to be hoped that the visual aspect of the safety problem will be given immediate attention. In this, the suggested board of ophthalmologists should be able to give invaluable assistance as consultants.

Comment: The Center for Safety Education of New York University and the New York University Medical Center held a symposium in the last year on the "Medical Aspects of Motor Vehicle Accident Prevention." The Committee on Visual Standards under the chairmanship of Dr. Conrad Berens made its report on this occasion on much the same problems discussed in Dr. Guerry's paper. A resumé on the recommendations of this committee will serve as best comment to it. The committee recommended that the usual three categories of public transportation, interstate commerce, and private car operating be changed and that the first two be combined. In this group, visual acuity is to be correctible to 20/30 in each eye and if glasses are needed an extra pair should be mandatory. Form fields should be 70 degrees in the horizontal meridian in each eye and 140 degrees for the pair of eyes. The committee has set no requirements for color vision but recommended that "the shape, size, position and color of traffic lights be standardized." It also

found that "no requirement for stereopsis (depth perception) is indicated." It recommended no test for light sense but suggested that "the presence of night blindness should be excluded by direct question." Yearly re-examination should be mandatory.

In the case of private operators the committee recommended that visual acuity be correctible to 20/40 in the better eye and that the form field requirements be either 70 degrees in the horizontal meridian in each eye or 140 degrees in one eye. Re-examination should be mandatory every 3 years.

The committee also dealt with the inequalities of the different state laws and with the design of cars, recommending that designers give special attention to such factors as windshield wipers, tinted windshields, reflection from chrome, mirrors, rear windows, etc. It made suggestions for the further study of reaction time, muscle balance and depth perception in their relationship to accidents and for the evaluation of fitness to drive in the case of drivers involved in accidents.

ARTHUR LINKSZ

Basic Sciences

ANATOMY

ANGLE OF ANTERIOR CHAMBER: FUNCTIONAL STRUCTURE OF CILIARY BODY IN SOME EXPERIMENTAL ANIMALS AND IN MAN

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The structures of the ciliary body and of the angle of the anterior chamber of the eye of various mammals were studied from functional points of view in preparations of membrane, micropreparations, and "thick sections" according to Dabelow's technique. A functional bipartition of the ciliary body was observed in domestic mammals (horse, cattle, sheep, goat, pig) and rabbits, and partly in some carnivorous mammals (cat, dog). The insertion of the ciliary muscle is situated far behind and consists of circular, intrascleral fibers for which the term "supporting fibers" has been coined, but the connective tissue body is considerably loosened by retiform spaces which contain aqueous humor and by a filtrating network (so-called scleral framework) which is rich in cells. The iris is fixed mechanically on the cornea mainly by the ligamentum pectinatum iridis. Schlemm's canal is missing since the scleral surface which absorbs the aqueous humor is very large.

Conditions are different in monkeys and human beings. The angle of the chamber is narrowed by a massive increase in size of the ciliary muscle, and the surface of absorption is concentrated to a small area. Fontana's spaces disappear to a great extent and Schlemm's canal develops. The ciliary muscle is displaced forward and assumes a functional relation with the structures of outflow. The anterior tendons of the muscle pass into the filtrating network of Schlemm's canal (so-called ligamentum pectinatum which, in contrast to the "iridis," should be called "corneoscleral"). Müller's muscle, which with its tendons builds up an elastic fibrous ring in the area of the root of the iris, takes over the fixation of the iris. Thus the burden is taken off the ligamentum pectinatum iridis and it is reduced morphologically. In man, there remains only a tender collagenous framework which serves as a base for a closed endothelial membrane for which the term "membrane iridocornealis" is suggested; this membrane covers the angle of the anterior chamber. Only the trabeculum cornosclerale shows larger pores (with a sagittal diameter of from 6 to 9 μ on the average) which are partly covered by the endothelial layers. There is apparently a rela-

tionship between the reduction of the endothelium of the iris (which begins in the monkey) and the narrowing of the angle of the anterior chamber by the increase in the size of the muscle (increased accommodation) and by unification of the ciliary body.

Comment: This work on the comparative anatomy of the angle follows closely that of Troncoso. Although the authors indicate that Schlemm's canal develops only with the primates, some of their illustrations show structures which certainly appear to be analogous. They also distinguish between ligamentum pectinatum iridis and ligamentum pectinatum corneoscleral. These terms add confusion since the ligamentum pectinatum iridis is the term we use for rudimentary pectinate ligament and the ligamentum pectinatum corneoscleral refers to corneoscleral trabeculum.

H. Saul Sugar

BACTERIOLOGY AND VIROLOGY

SYMPOSIUM: VIRAL KERATOCONJUNCTIVITIS

Sponsored by the National Institutes of Health, September 7 and 8, 1956

San Francisco, California

SUMMARY

Phillips Thygeson and Ernest Jawetz

Am. J. Ophth., 1957, *43:* (Pt. 2) 161–166

The following is an attempt to summarize briefly the principal areas of agreement and of difference among the workers in this field as brought to light in the course of the symposium, and to pinpoint the unsolved problems upon which further work must be done.

PHARYNGOCONJUNCTIVAL FEVER

Clinical Picture. The symposium focused attention on the clinical features of pharyngoconjunctival fever (PCF), particularly with respect to corneal changes. There was general agreement among the ophthalmologists that the conjunctival manifestation is an acute follicular conjunctivitis without pseudomembranes, characterized by a scanty, predominantly mononuclear cell exudate, an associated mild preauricular adenopathy, and a short course. It was agreed that the disease is clinically indistinguishable from the conjunctivitis of Newcastle disease or the acute follicular conjunctivitis known as "acute follicular conjunctivitis, Beal."

There was some difference of opinion on the frequency and nature of the corneal changes of pharyngoconjunctival fever but agreement that the original descriptions of the disease by Bell, Rowe, Engler, Parrot, and Huebner, and by Ryan, O'Rourke, and Iser, which stated that no corneal changes occurred, must now be modified. The University of California group maintained that the corneal changes were primarily epithelial, with only a very occasional transient subepithelial infiltrate, and that they bore little resemblance to the prominent, often grossly visible subepithelial infiltrates of epidemic keratoconjunctivitis. The University of Toronto group, on the other hand, reported that some of their cases of pharyngoconjunctival fever had lesions indistinguishable from those of epidemic keratoconjunctivitis.

There was general agreement among both ophthalmologists and virologists that, although sporadic cases might offer a problem in differential diagnosis, under epidemic conditions pharyngoconjunctival fever could be readily distinguished from epidemic keratoconjunctivitis. Huebner, for example, on the basis of extensive experience with pharyngoconjunctival fever, said that he had never seen a case of typical epidemic keratoconjunctivitis and that none of the inoculations made by the National Institutes of Health group with adenovirus 3 had resulted in a condition resembling epidemic keratoconjunctivitis. Ryan stated that he had only once seen a case of pharyngoconjunctival fever with keratitis and that it was a transient manifestation. It was recalled that Cockburn, who is not an ophthalmologist, had no difficulty distinguishing cases now known to have been pharyngoconjunctival fever from the cases of epidemic keratoconjunctivitis he saw in the Kansas City epidemic; and that during the 1950 and 1951 epidemics of pharyngoconjunctival fever in children that occurred in the San Francisco Bay region, epidemic keratoconjunctivitis was not considered in the differential diagnosis because of the absence of typical corneal lesions.

There seemed to be agreement that pharyngoconjunctival fever had existed in the United States prior to World War II but that epidemic keratoconjunctivitis was probably introduced in 1941 in connection with the war effort.

There was general agreement as to the identity, both clinical and serologic, of pharyngoconjunctival fever and the conjunctivitis described by Cockburn under the name "Greeley conjunctivitis." In connection with the suggestion that the so-called "acute follicular conjunctivitis, Beal" might also be identical with pharyngoconjunctival fever, it was recalled that in about one-third of Beal's original cases there was an associated upper respiratory disease. Beal made no reference to swimming pool transmission but later observers have done so. The finding of corneal changes in Beal's conjunctivitis has not been reported, however, and further work must be done before certain identification of the two diseases can be made. It may be that corneal changes have not been reported because of incomplete slit lamp studies.

Epidemiology. All observers have noted apparent transmission of pharyngoconjunctival fever through swimming pools and the highest incidence of the disease in the summer months. In discussion, however, Huebner questioned the role of the swimming pool as a transmitter of the virus, suggesting rather that

swimming tended to traumatize the conjunctiva and thus to favor infection which might otherwise be resisted. This factor, of importance in epidemiology, certainly needs further study, particularly as to the survival of adenovirus in chlorinated and unchlorinated water. It is noteworthy that no one has reported the occurrence of office epidemics of pharyngoconjunctival fever. This is in marked contrast to the high incidence of epidemics of epidemic keratoconjunctivitis in offices, hospitals, and dispensaries. This difference and the apparent predilection of pharyngoconjunctival fever for children could be explained by the high incidence of antibody to type 3 adenovirus in the general population and the low incidence of antibody to type 8.

Etiology. While it is clearly established that adenovirus type 3 is the usual cause of epidemic pharyngoconjunctival fever in children, other types have been encountered in sporadic cases and family outbreaks. These include types 2, 3, 6 and 7. There was general agreement on the frequent association of certain types of adenovirus with certain disease pictures, as well as on the ability of many types to produce similar pictures.

EPIDEMIC KERATOCONJUNCTIVITIS

Clinical Picture. There was general agreement among the participants of the symposium that the main features of epidemic keratoconjunctivitis consisted of (1) an acute follicular or pseudomembranous conjunctivitis, depending on the severity of the disease, with adenopathy; and (2) a keratitis in the form of typical round subepithelial infiltrates, with onset a week or 10 days after the onset of the conjunctivitis, and of long duration. It was agreed that the conjunctival changes are usually much more severe and long lasting than those of pharyngoconjunctival fever; in the latter, for example, pseudomembranes never have been observed. In a paper contributed to the symposium by Pillat, epidemic keratoconjunctivitis is clearly differentiated from nummular keratitis, a disease common in Europe but seen rarely, if ever, in the United States.

It was maintained by the University of California group that the corneal changes of epidemic keratoconjunctivitis are readily distinguishable from those of pharyngoconjunctival fever on the following grounds: (1) That the infiltrates of epidemic keratoconjunctivitis are usually grossly visible while those of pharyngoconjunctival fever are usually visible only with the slit lamp; (2) that the lesions of epidemic keratoconjunctivitis are primarily subepithelial while those of pharyngoconjunctival fever are primarily epithelial; and (3) that when corneal changes occur in pharyngoconjunctival fever they appear at the same time as the conjunctival changes, while in epidemic keratoconjunctivitis they are delayed from 7 to 10 days. Another difference mentioned was that permanent visual damage is known to have been caused occasionally by epidemic keratoconjunctivitis but never by pharyngoconjunctival fever.

It was agreed that an apparent predilection for children has been shown by pharyngoconjunctival fever but not by epidemic keratoconjunctivitis. It was further agreed that except in children epidemic keratoconjunctivitis is usually not associated with systemic signs of any kind. This is in marked contrast to

pharyngoconjunctival fever which is regularly associated with systemic signs. According to Dr. Tanaka's report, however, epidemic keratoconjunctivitis in children has displayed severe systemic signs consisting of high fever, pharyngitis, otitis media, diarrhea, and vomiting. She refers to Mitsui's experiments in which transmission of material from this infantile form of the disease produced typical epidemic keratoconjunctivitis without such systemic signs in adults. If this transmission experiment had not been made, one would be tempted to believe that the children had had primary herpetic keratoconjunctivitis which is known to be accompanied by severe systemic signs and in which the conjunctival signs are similar to those of epidemic keratoconjunctivitis. Some of these children have been shown to have rises in adenovirus type 8 antibody.

Noteworthy to Dr. Tanaka's report is her statement that, until recently, epidemic keratoconjunctivitis and pharyngoconjunctival fever have been confused in Japan. This is reflected particularly in the reports of swimming pool transmission. Further study is definitely indicated to determine how frequently epidemic keratoconjunctivitis spreads through swimming pools.

Epidemiology. All participants in the symposium agreed that epidemic keratoconjunctivitis is highly communicable and pharyngoconjunctival fever somewhat less so. It was brought out that in the United States, swimming pool transmission has been typical of pharyngoconjunctivitis, that transmission in hospitals, dispensaries, and private offices has been characteristic of epidemic keratoconjunctivitis but unknown with pharyngoconjunctival fever, and that epidemic keratoconjunctivitis has had a marked tendency to spread among professional personnel and pharyngoconjunctival fever has not. In the San Francisco Bay area, for example, two sporadic cases of pharyngoconjunctival fever in general physicians were studied, but in the course of two major epidemics of the disease, primarily among children, in this same area, no instance of its transmission to ophthalmologists or pediatricians was noted in spite of the many hundreds of cases that developed. Epidemic keratoconjunctivitis, on the other hand, spreads with ease through hospitals and so forth, and has affected numerous ophthalmologists. That it can be a serious public health problem was re-emphasized by Dr. Leopold's report of a recent hospital epidemic among postoperative patients.

The role of trauma, particularly industrial trauma, and the connection between foreign body removal and epidemic keratoconjunctivitis, were discussed at length. It was interesting that in the Schenectady epidemic Dr. Korns found no significant difference in the opacities or clinical severity of cases apparently contracted in the eye clinic, after foreign body removal, and of cases infected subsequently as a result of household contacts. In an unpublished study of 32 ophthalmologists who contracted the disease while treating patients, it was found that all had corneal opacities and that the only conceivable trauma had been the simple rubbing of the eyes with the fingers. In a number of these cases the disease was very severe. The role of trauma in transmission and its effect on the severity of the disease and the incidence of opacities are certainly still in doubt.

In none of the studies of epidemic keratoconjunctivitis and pharyngoconjunc-

tival fever has any instances of a second infection with either disease in the same individual been noted. Apparently both diseases confer a definite and lasting immunity.

Etiology. Whether any type of adenovirus except type 8 has been found associated with typical epidemic keratoconjunctivitis is open to some doubt. The evidence listed below supports the contention that adenovirus type 8 is at least one agent capable of causing the picture typical of epidemic keratoconjunctivitis. Some confusion has arisen because certain observers have recorded keratitis of minor degree and short duration in the course of adenovirus type 3 and type 7 infections. Considering the spectrum of any disease caused by a specific etiologic agent, it appears natural that in addition to typical full-blown cases there will be many marginal ones lacking certain diagnostic features. The typical cases are the only ones that can be diagnosed initially until the etiologic agent has been established. When this has been accomplished, atypical cases can be diagnosed by laboratory means. At the present time the evidence suggests that types of adenovirus other than type 8 have not given rise to the typical diagnostic subepithelial opacities, and that overlapping therefore exists mainly between atypical epidemic keratoconjunctivitis (associated with adenovirus type 8) and transient keratitis seen in infections due to other types.

The evidence pointing to adenovirus type 8 as at least one of the etiologic agents of typical epidemic keratoconjunctivitis can be summarized as follows:

(1) Three strains of adenovirus type 8 have been isolated to date, all from eye lesions. This type of adenovirus has not been recovered from other sources. Adenovirus type 8 differs biologically from other adenovirus types, particularly in its exceedingly low infective titer for tissue culture cells compared to the relatively large amount of noninfective virus (antigenic material present.)

(2) Of 70 patients with the definite clinical diagnosis of epidemic keratoconjunctivitis in the United States, Canada, Switzerland, Italy, and Japan during 1951–55, 66 or 94.3 per cent had neutralizing antibodies to adenovirus type 8 in a serum dilution of 1:10 or greater. Of 140 individuals from the same geographic areas and similar age groups who did not have clinical epidemic keratoconjunctivitis, only 10 or 7.1 per cent had such antibodies. In an epidemic in Austria in 1952–53 from which sera were collected three years later, the incidence of 1:10 antibodies to adenovirus type 8 was 52.4 per cent in epidemic keratoconjunctivitis and 13.3 per cent in controls.

(3) Of 17 adequately paired sera available from patients with typical epidemic keratoconjunctivitis in Chicago, California, and Japan, 15 developed a fourfold or greater rise in neutralizing antibodies to adenovirus type 8 during their illness. Unfortunately, there was much variation in the highest titers reached by these individuals and in the length of time such antibody titers persisted. In all individuals followed through the course of adenovirus type 8 infection of the eye, the antibody titer did not exceed 1:20 two years after onset of the infection. Thus retrospective serologic investigations are virtually impossible, unless sera from typical cases have been obtained within one year of onset and properly stored thereafter.

(4) Patients with epidemic keratoconjunctivitis who exhibited a marked

antibody titer rise against adenovirus type 8 did not have such titer rises for other types of adenovirus, for herpes simplex virus, or for the "E.K." strain of St. Louis encephalitis virus.

(5) Adenovirus type 8 was inoculated into one eye of each of five volunteers. Four developed typical epidemic keratoconjunctivitis; the fifth had specific antibodies to adenovirus type 8 at the time of inoculation and remained well. The uninoculated eye became involved in three volunteers 6 to 8 days after the inoculated eye. Adenovirus type 8 was re-isolated from the lesions and the volunteers developed significant antibody titer rises. Work is currently in progress to establish whether vaccination of volunteers with adenovirus type 8 will prevent the development of epidemic keratoconjunctivitis upon subsequent inoculation of the eye with the agent.

The position of the so-called "Sanders virus" of epidemic keratoconjunctivitis was discussed at length. This agent was originally implicated in the epidemic keratoconjunctivitis epidemics of 1940–42. At that time it was isolated repeatedly by Dr. Murray Sanders from typical cases and gave serologic reactions with these patients' sera. The subsequent fate of this virus is not known, but in 1947 the agent carrying the label of "EKC virus"—perhaps derived from the original isolation—was a variant of St. Louis encephalitis virus and had no serologic relationship to the epidemic keratoconjunctivitis cases which occurred between 1947 and 1955. While there was much speculation concerning this confusing situation, no final solution to the riddle was forthcoming. It was felt that an exact repetition of the efforts of Dr. Sanders in 1940 was not indicated because of the high probability that in repeated animal passage a latent virus would be "picked up" accidentally. This has already occurred in the hands of some workers. Thus it was concluded that (a) the nature and fate of the original "Sanders virus" remains uncertain, and (b) the strains of that virus currently available bear no evident relationship to the disease epidemic keratoconjunctivitis as it exists at the present time.

The following points should be pursued in order to establish the etiology of epidemic keratoconjunctivitis on firm ground:

(1) In epidemics occurring in various parts of the world, *entirely typical* cases should be studied by virus isolation and antibody titer determinations.

(2) Additional volunteers should be inoculated with the recovered agents, their clinical and serologic responses should be noted and the viral agent re-isolated.

(3) In serologic surveys, the incidence of specific antibodies to isolated agents should be compared in *typical* and *atypical* cases diagnosed as epidemic keratoconjunctivitis, in other eye diseases, and in comparable control populations.

(4) The agents isolated in various parts of the world should be exchanged by different laboratories in efforts to obtain confirmation of results.

HERPETIC KERATITIS AND KERATOCONJUNCTIVITIS

There was general agreement that the problems of herpetic keratitis and conjunctivitis have become more important since the war and since the introduction of cortisone and related steroids for topical use in ocular infections.

There seemed to be general agreement that primary herpetic infection of the eye may occur in children as a severe keratoconjunctivitis but that, in the secondary forms, the conjunctiva is usually spared and the cornea alone involved. It was also agreed that herpetic keratitis appears typically as a dendritic keratitis but that a variety of other superficial and deep forms can occur, and that of these the most important is the so-called "hypopyon keratitis" whose exact nature needs elucidation. The consensus was that the majority of cases of hypopyon develop as a result of secondary bacterial or mycotic infection, but the University of California group felt that, at least in certain cases, the action of herpes simplex virus alone is responsible. Further investigation of the nondendritic forms of herpetic keratitis is much needed.

There was discussion of the possibility that some cases of dendritic keratitis in adults may represent primary infection. In view of the paucity of available evidence, however, no conclusion could be reached. The problem needs further serologic work.

The role of steroid therapy in the development of chronicity and other complications in herpetic keratitis was then discussed. There seemed to be general agreement that the widespread topical use of the steroid hormones has contributed to the relatively high frequency of complications noted in the postwar years. Further experimental work is needed to determine whether this effect is due to increased proliferation of virus in the tissues or to an unfavorable effect on the tissues themselves.

Among the many questions that were raised and left unanswered concerning immunity in herpetic keratitis and conjunctivitis, two of the more important were: (1) Does the presence of antibodies protect the conjunctiva from involvement in corneal relapses? (2) When a conjunctivitis occurs in a relapse, as occasionally happens, does this always indicate the presence of secondary infection with bacteria or other agents?

It was agreed that herpes simplex virus could be isolated with great ease from typical epithelial corneal lesions early in the disease, but only with great difficulty and infrequently from stromal lesions, and that it is isolated very infrequently in the absence of clinical herpetic disease. Its possible presence in the "latent stage" in the eye could thus lead to confusing laboratory results. The meaning of "latency" in herpes simplex and the problems concerned with the unmasking of latent viruses were discussed in detail.

Many questions dealing with primary infection versus recurrence were also examined. Does a recurrence always indicate that the same tissue area was involved in the primary infection? May a dendritic keratitis occurring for the (apparently) first time late in life be a primary infection, or is it always a recurrence of an infection 20 or 30 years before? In "latency" is the virus in an incomplete ("provirus") form requiring activation by the trigger mechanism to become infective, or is there infective virus present within certain cell groups which spreads when the close symbiotic relationship is disturbed by the trigger? Is the infection with herpes virus so strictly limited to the corneal epithelium that its total removal by curettage, or in the course of corneal grafting, may lead to permanent security from relapse?

The lack of unanimity of opinion on these questions suggested an urgent need for further investigative work.

Comment: Modern tissue culture techniques have made possible the major advances in the isolation and identification of viruses described in this significant progress report. Great credit belongs to the participating ophthalmologists for the important contributions they have made to the field of virus research through utilization of these newer methods. Especially noteworthy is the cooperative effort toward the solution of common problems evidenced by the participation of virologists, epidemiologists and ophthalmologists in studies reported in this symposium.

Although the identification and typing of viruses remains a research problem beyond the scope of ordinary ophthalmic practice, there are signs that isolation of viruses from ocular infections may some day be possible with little greater difficulty than that involved in taking bacterial cultures from the eye. Beale, Doane and Ormsby have reported in this symposium the use of human amnion cells for isolation of an adenovirus frim the eye. In recent months, working at the Children's Medical Center and the Massachusetts Eye and Ear Infirmary, Kaufman and Kaufman have found human amnion cells a superior medium for isolation of adenoviruses and of herpes simplex from ocular infections. Ease of maintenance, length of storage and rapidity of virus growth are some of the advantages they cite for human amnion cells over HeLa cultures and other methods.

Although the recent findings are of the greatest diagnostic interest, practical problems of treatment and prevention remain. There is reason to hope that means of specific treatment will evolve from basic studies of viruses in tissue culture. Vaccine prophylaxis, now firmly established for poliomyelitis, may become a reality for ocular virus infections. In the meantime, ophthalmologists should concentrate upon (1) avoidance of medications which do more harm than good and (2) elimination of the possibility that they or their instruments may continue to serve as vectors for the spread of infectious disease.

HENRY F. ALLEN

BIOCHEMISTRY

RATE OF SECRETION OF AQUEOUS HUMOR

BERNARD BECKER

The Second Edward Lorenzo Holmes Memorial Lecture of the Institute of Medicine of Chicago, Chicago, Illinois

Tr. Inst. Med. Chicago, 1957, *36:* 195–200

Because of the important finding of carbonic anhydrase in the cilairy body (Wistrand), the excess of bicarbonate and the higher pH in the aqueous humor (Kinsey), it was possible to presume that carbonic anhydrase inhibitors, such as acetazoleamide, would affect the secretion of aqueous. The fact that this agent proved to decrease significantly the rate of formation of aqueous humor in patients made available a new agent for the therapy of the glaucomas.

The application of carbonic anhydrase inhibitors to animals has opened a new chapter in the study of aqueous humor dynamics. For the first time one could alter the rate of secretion and determine the changes induced in composition and dynamics of the aqueous humor. The development of tonography (Grant), perfusion techniques (Barany), and a solid theory of aqueous humor dynamics (Friedenwald and Becker) made it practical not only to measure the rate of aqueous secretion, but also to determine its modifications as measured by these methods following carbonic anhydrase inhibition. Most important have been the possibilities afforded for comparison of several independent approaches to the absolute and relative measurements of rate of aqueous flow before and after acetazoleamide.

Relative methods of measurement of rate of aqueous secretion include the semiquantitative fluorescein appearance time as well as the more precisely determined alterations in static chemistries. Absolute measurements of aqueous flow are derived from the determination of intraocular pressure and facility of outflow by perfusion or tonographic studies or from the laborious estimates obtained from the rate of turnover of test substances. It is the purpose of this presentation to review and compare the results obtained by these methods in animal and human eyes.

Fluorescein Appearance Time. The appearance time of fluorescein through the pupil into the anterior chamber after its intravenous administration has been proposed by Friedenwald and co-workers as a measure of the rate at which aqueous enters the eye. If one measures the difference in appearance time in the conjunctival vessels and in the pupillary space, one has an estimate of time of transit from the ciliary body to the anterior chamber. There are enormous variations in this time among different eyes and it cannot be interpreted in absolute terms. However, repeated determinations in the same eye are quite

reproducible and alterations in appearance time can be interpreted as relative changes in rate of aqueous flow. Following the administration of acetazoleamide to animals or patients, a marked delay in appearance of fluorescein was observed. As a first approximation, aqueous flow may be assumed to be inversely proportional to fluorescein appearance time. One may then attempt to quantitate alteration in flow as follows:

$$\text{fluor } \% = 100 \frac{T_{\text{fluor}_1} - T_{\text{fluor}_2}}{T_{\text{fluor}_2}} \tag{1}$$

where fluor % is the per cent change in rate of aqueous flow, T_{fluor} is the time interval between the appearance of fluorescein in conjunctival vessels and its appearance through the pupil into the anterior chamber, 1 is before administration of drug, and 2 is after administration of drug.

Attempts at using the above quantitative formulation before and after Diamox administration revealed that in a series of 22 rabbits the decrease in rate of aqueous flow produced by Diamox averaged 49 per cent. Similar tests applied to 16 human eyes after 500 mg. of Diamox indicated an average suppression of aqueous flow of 54 per cent.

Static Chemistries. The concentration of a substance in the anterior chamber (C_{AC}) at time (t) has been formulated in the following terms:

$$\frac{dC_{AC}}{dt} = K_P C_{PC} + K_D (C_{Pl} - C_{AC}) - K_P C_{AC} \tag{2}$$

where K_D is the coefficient of transfer by diffusion between plasma and anterior chamber, K_P is the coefficient of transfer by flow into and out of the anterior chamber, C_{PC} is the concentration in posterior chamber, and C_{Pl} is the concentration in plasma. At equilibrium $\frac{dC_{AC}}{dt} = 0$. Under these steady state conditions:

$$\frac{K_P}{K_D} = \frac{C_{AC} - C_{Pl}}{C_{PC} - C_{AC}} \tag{3}$$

The steady state concentrations of constituents of the plasma and aqueous humor of posterior and anterior chambers thus provides a measure of K_P/K_D. Although this does not determine absolute values for the rate of flow (K_P), alterations in the ratio may be measured following carbonic anhydrase inhibition. These measurements have proved reasonably valid since acetazoleamide did not affect the rate of diffusion (K_D) significantly. The alterations in steady state concentrations of bicarbonate and ascorbate have been determined in rabbit eyes. The results of such studies revealed an estimated decrease in rate of flow in rabbit eyes averaging 64 per cent for bicarbonate (24 rabbits) and 60 per cent for ascorbate (28 rabbits). When 15 rabbits were saturated with ascorbate, the alteration in this new steady state concentration by Diamox was consistent with an average decrease in flow of 51 per cent. Thus, values for

relative changes in rate of aqueous secretion following Diamox as measured by the steady state concentration method are quite consistent for different substances. Furthermore they appeared to agree reasonably well with fluorescein appearance time data.

The Facility of Outflow. As first suggested by Goldmann, the rate of flow of aqueous humor is proportional to the outflow pressure gradient between the anterior chamber and the episcleral veins. The proportionality constant has been labelled C, the coefficient of facility of outflow. Thus,

$$F = C(P_o - P_v) \tag{4}$$

where F is the rate of flow (cu. mm./min.), P_o is the intraocular pressure (mm. Hg), P_v is the episcleral venous pressure (mm. Hg), and C is the coefficient of facility of outflow. The facility of outflow can be readily determined from perfusion studies. Thus, in the cannulated enucleated eye, human or animal, one may set the pressure of perfusion (P_I), and measure the rate of inflow of saline (I) from the cannula. Then:

$$I = C \times P_I \tag{5}$$

where I is the rate of perfusion (cu. mm./min.) and P_I is the infusion pressure (mm. Hg). When corrected for temperature alterations, the measurement of rate of inflow from the cannula (I) divided by the pressure of perfusion provides an accurate *in vitro* estimate of the facility of outflow (C).

The perfusion method may also be applied to the eye of the living animal (and occasionally the human eye) preceding enucleation. Under these circumstances,

$$I = C(P_I - P_o) \tag{6}$$

where P_o = intraocular pressure in the undisturbed eye and I and P_I are determined as in (5). By plotting the data obtained for I against the various set values for P_I, one obtains excellent straight lines. The slopes of such plots provide a value for C; the intercept at zero inflow estimates P_o, and the intercept at a pressure equal to episcleral venous pressure provides a value for rate of secretion of aqueous. In 60 normal rabbit eyes, average values so obtained were P_o = 19 mm. Hg; C = 0.35; and flow = 3.5 cu. mm./min. by this method of measurement.

Tonography provides a more practical method for measuring facility of outflow (C) and intraocular pressure (P_o) in the living eye. This technique has proved most useful in glaucoma diagnosis and therapy. It involves the continuous recording for 4 minutes of the pressure within the eye (P_t) with a tonometer in place. As formulated by Grant:

$$C = \frac{V}{4\,(P_t - P_o)} \tag{7}$$

where V is the volume of fluid expressed from the eye by the tonometer in the 4 minutes of application and P_o is the intraocular pressure in the undisturbed

eye. By means of such tracings it has been possible to measure C and P_o in both rabbit and human eyes. From equation (4) flow rates may then be computed. Average normal values for 90 rabbits have revealed $P_o = 20$; $C = 0.33$; and flow = 3.6 cu. mm./min. For 175 normal human eyes an average P_o of 17 mm. Hg; C of 0.31; and flow of 2.2 cu. mm./min. were obtained. This estimate for flow in human eyes is in remarkably good agreement with the average value (2.3 cu. mm./min.) obtained by Goldmann from fluorescein turnover studies.

The changes induced in these flow values as measured by tonography following the administration of carbonic anhydrase inhibitors have been extensively studied. Thus, in 84 human eyes acetazoleamide administration resulted in an average suppression of secretion of 55 per cent. In 66 rabbit eyes aqueous flow was reduced by an average of 61 per cent following Diamox. These average values were in excellent agreement with the mean values obtained by the other independent measurements discussed above. Furthermore, tonography could be compared with other methods in more critical and precise fashion by applying several methods to the *same eye*. Thus, the alterations in flow following systemic carbonic anhydrase inhibition have been measured by both the changes in tonography and bicarbonate concentrations on the same rabbit. Such unrelated methods gave results within approximately 10 per cent of one another. Fluorescein appearance time has been compared with tonography on the same human eye with less than 15 per cent variation in estimates between methods. Perfusion measurements *in vivo* and *in vitro* have been correlated with tonography on the same eyes in a large number of rabbits and in a few patients. Agreement has been excellent and well within the experimental errors of the procedures (8 to 15%).

An interesting sidelight of the facility of outflow measurements before and after a single dose of acetazoleamide has been the tendency for compensatory changes. Thus when secretion of aqueous has been partially supressed, decreases in intraocular pressure are induced. However, intraocular pressure in human and rabbit eyes is usually restored partially or completely before there is recovery of aqueous secretion. This is accomplished by a temporary decrease in facility of outflow, thus raising intraocular pressure in spite of depressed secretion.

Turnover of Test Substances. The measurement of turnover of such test substances as ascorbate in the aqueous humor of posterior and anterior chambers provides one of the most precise, but laborious, methods of estimating aqueous flow. By maintaining plasma ascorbate at 15 to 20 mg. per cent and analyzing posterior chamber and anterior chamber samples of large numbers of animals at frequent intervals from 5 minutes up to 18 to 24 hours, one can determine the rate of secretion of aqueous. Paired experiments on animals receiving acetazoleamide provide flow rates for comparison. From equation (2) it is apparent that

$$\frac{\frac{dC_{AC}}{dt}}{C_{PI} - C_{AC}} = \frac{K_F\,(C_{PC} - C_{AC})}{C_{PI}\,C_{AC}} + K_D \qquad (8)$$

This is an equation of the formula:

$$Y = K_F X + K_D \tag{9}$$

where $Y = \dfrac{\dfrac{dC_{AC}}{dt}}{C_{PI} - C_{AC}}$

$$X = \frac{C_{PC} - C_{AC}}{C_{PI} - C_{AC}}.$$

The turnover data for concentrations in posterior chamber, anterior chamber, and plasma furnished estimates for Y and X at different times after the injection of ascorbate. Plotting Y vs. X resulted in a straight line with slope of K_F, the flow constant and Y intercept of K_D the diffusion constant. In normal rabbits the values obtained by this method were $K_F = 0.0175$; $K_D = 0.0045$. Diamox treated animals had K_F reduced to 0.0085 (51 per cent supression of flow), but K_D was essentially unchanged (0.0040). At an anterior chamber volume of 200 cu. mm., these flow rates would correspond to approximately 3.5 cu. mm./min. in the normal rabbit and 1.7 cu. mm./min. after carbonic anhydrase inhibition. Thus, the absolute rate of flow in the normal rabbit eye as measured by this method agreed very well with the tonographic estimate (3.6 cu. mm./min.) and the perfusion data (3.5 cu. mm./min.) for rabbits. Furthermore, the estimated decrease in flow following carbonic anhydrase inhibition was quite comparable to the other measurements.

The diverse approaches to the problem of estimating the rate of secretion of aqueous humor and its alteration by acetazoleamide, as presented in this paper, are summarized in Table 1. The excellent agreement obtained by such completely independent methods of measurement, each with its own assumptions and errors, strongly suggest the basic validity of current concepts of aqueous

TABLE 1

Comparison of Methods for Estimating the Alteration in Rate of Secretion of Aqueous Induced by Acetazoleamide

Experiment	No.	Per Cent Decrease
Fluorescein appearance time		
Rabbits	22	−49
Human	16	−54
Static chemistries (rabbits)		
Bicarbonate	24	−64
Ascorbate	28	−60
Saturated ascorbate	15	−51
Facility of outflow		
Rabbits	66	−61
Human	84	−55
Turnover of test substances (rabbits)		
Ascorbate	—	−51

humor dynamics and methods of measurement of the rate of formation of aqueous humor.

Comment: This paper was given on the occasion of the second Edward Lorenzo Holmes Memorial Lecture. The prize was established by the son of this distinguished Chicago ophthalmologist and is awarded each year by the Institute of Medicine of Chicago to a young man who has made a significant contribution to medicine. The donor specified that if possible the award by made to an ophthalmologist, and up to this time (the Third Annual Award will be made on May 20th) it has been unnecessary to seek outside the ranks of the ophthalmologic world for a worthy recipient.

As is well known to most students of the eye, Dr. Becker, on the basis of Friedenwald's theory of aqueous secretion, predicted that a carbonic anhydrase inhibitor, such as acetazoleamide (Diamox), would decrease the rate of aqueous formation. This hypothesis was confirmed experimentally and clinically and a brilliant new epoch in the treatment of glaucoma launched.

However some workers in the field are still skeptical of the primary function of carbonic anhydrase in aqueous formation. They feel that the conversion of CO_2 and water to carbonic acid is only one step in the complex mechanism of aqueous formation (See Davson, *Physiology of the Ocular and Cerebrospinal Fluids*, p. 334). In this article, Dr. Becker gives a partial answer to these critics. He has measured the secretory rate of aqueous by four different methods: fluoroscein appearance time, concentration of bicarbonate and ascorbate in the aqueous, tonography and turnover rate of ascorbate. In each case administration of Diamox reduced the secretory rate 50 to 60 per cent. He thus concludes that no matter what test method is used, one can demonstrate that carbonic anhydrase is necessary for the formation of aqueous. As a corollary, there is no implication here that other enzymes present in living tissue such as those necessary for glycolysis and respiration are not present in the ciliary body. Nor is there any doubt that any general protoplasmic poison will interfere with the function of this structure. However, in light of the evidence presented by Dr. Becker, a specific role for carbonic anhydrase is difficult to deny.

DAVID SHOCH

TOTAL ASCORBIC ACID IN AQUEOUS HUMOR AND SERUM IN INDIAN PATIENTS WITH AND WITHOUT CATARACT

ITS PHYSIOLOGIC SIGNIFICANCE

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A. M. A. Arch. Ophth., 1956, *56:* 756–760

The total ascorbic acid concentration in aqueous (comprising two components —the reduced form as *l*-ascorbic acid, and the oxidized product, as dehydro *l*-ascorbic acid) although very variable, is much higher than that in blood

plasma. In various animals, including man, the concentration ratio is about 6–8:1. Moreover, it has recently been found that the concentration of ascorbic acid in the aqueous humor varies approximately as the concentration in the serum, regardless of whether or not the lens is cataractous, the subjects of the investigation having been normal patients, aphakic patients, and patients whose lenses were sufficiently opaque to warrant extraction. A comparative study was therefore made of total ascorbic acid in aqueous and serum of 13 Indian patients of three categories: (1) with normal lenses, (2) with different types of cataract, and (3) without lenses as a result of previous extraction. The patients accepted for study included 8 with various types of cataract, 2 with aphakia, 1 with aphakia accompanied by onset of phthisis bulbi due to postoperative endophthalmitis, and 2 with normal lenses.

Study of the ascorbic acid content found in the aqueous and serum of the patients examined showed no very wide variations in concentration. The ratio of ascorbic acid content in aqueous to that in serum was more or less the same in persons with cataractous lenses or with aphakia, although the ascorbic acid content in the aqueous increased with that of the serum. The ratio in patients with normal lenses was rather low, but that in the patient with phthisis bulbi was definitely higher. Analysis of the total ascorbic acid content showed that in general the concentration of this substance in aqueous is always higher than that in serum. There are three possible explanations for the higher concentration in the aqueous: (1) Direct synthesis of the ascorbic acid by the lens; (2) the ascorbic acid enters the eye from the blood in the oxidized form, which is reduced by the lens and accumulates in the aqueous because of the supposed comparative impermeability of the blood-aqueous barrier to the reduced form; and (3) secretion of ascorbic acid by the ciliary epithelium.

If the lens is responsible for the higher concentration of ascorbic acid in the aqueous, it must produce it through some metabolic process characteristic of itself. The results in this study, however, show that both in cases of total cataract, in which the metabolism of the lens was completely stopped, and in cases of very early cataract with a large number of lens fibers still remaining transparent in which there was every probability that the metabolism was still going on, the concentration was higher in the aqueous and at about the same level in the two conditions. Even in cases of aphakia, in which there were very few lens fibers left, the result was the same. These findings corroborate the conclusions of earlier observers and provide strong evidence against the theory that the lens is responsible for maintaining a higher concentration of ascorbic acid in the aqueous.

The part played by the ciliary epithelium in maintaining the higher concentration of ascorbic acid in the aqueous is not yet definitely known. The ratio of ascorbic acid in aqueous to that in serum in the patients with cataractous lenses was strikingly low as compared with the ratios found by other workers. The low ratio was the result of a lower ascorbic acid content in the aqueous. Now, if the ciliary epithelium is at all responsible for the formation of the ascorbic acid in the aqueous, is it possible that the higher pigment content in the

ciliary epithelium of these patients, all of whom were colored people, may have exerted a retarding effect on the process, so as to explain the uniformly low ratio of the ascorbic acid content? One meager bit of evidence was found to support this theory, and that was the fact that in the patient with phthisis bulbi without a lens, the ratio was almost double. As there was still an anterior chamber and aqueous could be withdrawn, a part of the ciliary body was undoubtedly still functioning, but perhaps the pigment-containing epithelium, being the deeper layer, was the more seriously damaged, so that its retarding effect on the formation of ascorbic acid was lost. On the other hand, in a patient with Fuch's heterochromic cyclitis, the retarding effect of the pigment epithelium was unimpaired and the ratio of ascorbic acid was on the same level as in other cases. The ascorbic acid ratio in the two patients with normal lenses was very low, 2:6 and 1:3, but no explanation has been found to account for the fact.

Comment: It is firmly established that ascorbic acid is present in much higher concentration in the aqueous than in blood plasma (the ratio except in the cat, varying from 10/1 to 40/1). Originally it was felt that in some way the lens played a part in maintaining this unusual equilibrium. Recently, however, workers in Kinsey's laboratory (Arch. Ophth. *51:* 1, 1954) showed that a normal ratio prevailed in human cataractous eyes and even in aphakic eyes. This work is corroborated by the article abstracted above and should settle the problem. Unfortunately there is some good evidence to the contrary.

Laugham, in 1950, (J. Physiol., *111:* 388) found a much lower concentration of ascorbic acid in the aphakic eyes of rabbits as compared to the normal eye. Note that here the blood level was constant and at least four months had elapsed between the cataract extraction and the determinations of ascorbic acid in the aqueous.

It is difficult to reconcile these two sets of data unless one is willing to ascribe the discrepancy to the variation in experimental animal. A fundamental difference between man and rabbit in this regard is that only man (along with other primates and the guinea pig) is unable to synthesize his own ascorbic acid. This would seem to imply a lack of an enzyme or enzymes in man which may be the clue to the differential handling of ascorbic acid in the eye. A most exciting report in this regard recently appeared in Science (*124:* 1148, 1956). The authors point out that the rat can convert D-glucose to L-ascorbic acid via D-glucuronolactone and L-gulonolactone. The guinea pig on the other hand cannot synthesize L-ascorbic acid from L-gulonolactone. This defect in ascorbic acid synthesis is apparently due to the absence of the appropriate enzyme in the liver of the guinea pig. One may presume that a similar defect exists in man and it is interesting to speculate whether this difference gives rise to one set of data for man and the guinea pig and another equally reliable group of data for the rabbit.

DAVID SHOCH

OPTICS

FLICKER-FUSION THRESHOLDS

Comparison Between the Continuous and the Discontinuous Methods

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Determinations of the flicker-fusion frequency may be made by two fundamentally different procedures, the continuous or the discontinuous method. In the first, the frequency of the intermittent light source is altered evenly during the test period by a certain number of light flashes per second. In other words, the alteration of the frequency takes place with constant acceleration. Starting from a low frequency below the fusion limit and moving towards a higher one, the flicker-fusion threshold (t_{d-c}) can be determined by asking the observer to report when the visual impression changes from a flickering to a fused one. The fusion-flicker threshold (t_{c-d}) is determined by the reverse procedure, i.e., starting from a high frequency (above the fusion limit) and moving towards a lower one.

The discontinuous method, on the other hand, consists of the use of separate experiments in which the observer, during a given exposure time, is confronted with a constant frequency. In each experiment he is to report whether the visual impression is perceived as flickering or fused. From one experiment to another, the frequency is increased or decreased by, say, the interval of one light flash. The two thresholds may be determined by this method on the basis of the starting point, which may be either fused or flickering light.

In a previous paper, the author showed by the continuous method that the flicker-fusion threshold (t_{d-c}) and the fusion-flicker threshold (t_{c-d}) are affected in different ways by alterations in the experimental conditions, especially by alteration of the frequency acceleration. The t_{d-c} determination was highly dependent on this factor, but the t_{c-d} was not affected until the frequency acceleration reached such high values that the observer's reaction time became important. From this it seemed that the two thresholds must be assumed to reflect different functions of the eye and that they are, therefore, not comparable as claimed by Simonson and Brozek (1952).

The individual experiments were divided into three phases: (1) the flicker-fusion threshold (t_{d-c}) and the fusion-flicker threshold (t_{c-d}) were determined for an area of one size by the continuous method; (2) the same threshold values were then determined by the discontinuous method for exposure periods of 1, 3,

and 6 seconds; (3) both thresholds were then determined as in (1), and the mean value of the results obtained by (1) and (3) was taken to represent the t_{d-c} and t_{c-d} during the experimental period. Duplicate determinations of the continuous thresholds (i.e., before and after the discontinuous threshold determinations) were used to obtain a value representative of the individual experimental day, paying regard to the day-to-day variation in the flicker-fusion frequency and the decrease in the flicker-fusion frequency during prolonged exposure to flickering light previously shown to exist. This experimental plan was repeated on the third experimental day for the visual angle 1 degree and on the fifth experimental day for the visual angle 1.72 degrees. On the second, fourth, and sixth days items (1) and (3) were repeated for 0.46, 1.0, and 1.72 degrees respectively. On these days the procedure in (2) was altered so that the threshold value was approached from a light flash frequency which was above the fusion limit, i.e., the test patch was perceived as steady.

The experimental findings again confirmed the difference between the two flicker-thresholds determined by the continuous method, but the question of causal relationships remains open. One of the factors must be the varying perception of a physically constant frequency. Clarification of this factor, however, is difficult because of the existence of many inadequately investigated problems, such as the absence of firm fixation of the light source, local adaptation, and summation of after-images. The difficulties encountered in trying to fix the same point for some time are well known.

The fact, that t_{d-c} is not always numerically higher than t_{c-d}, previously demonstrated by the author, is further supported by the present experiments. The mutual situation of the continuous thresholds appears to depend, above all, on the method of accelerating the frequency. Moreover, the suggestion that the difference in the thresholds can be explained as a masked reaction period difference can no longer be maintained, because the results of the present study must be interpreted as follows: Because of its immediate relation to the discontinuous threshold determinations—which coincide whether the threshold is approached from flicker or from fusion—the continuous fusion-flicker threshold must be regarded as the continuous threshold which better reflects the ocular property of following the intermittence in a discontinuous light stimulus with varying frequency. The continuous flicker-fusion threshold also reflects this property, but the procedure used in its determination appears to contain elements that compromise it to a certain extent (summation of after-images, varying adaptation levels resulting from the continuously altered contrast).

The greater the contrast, the stronger and more prolonged will be the after-image. In fusion-flicker threshold determination there is, according to the experimental conditions, a fairly uniform, but at least constant, adaptation field which changes suddenly when the threshold has been reached. In flicker-fusion threshold determination, on the other hand, there is an adaptation field which at the outset shows marked contrast (low frequencies). During the experimental period the contrast is constantly varying, and this variation does not cease until the observer considers that the threshold has been reached. Pos-

sibly the difference in the situation of the thresholds can be explained by this continuously changing contrast with its resulting summation of after-images.

From this study it appears that discontinuous threshold determinations with a reasonable exposure period (5 or 6 seconds) or the continuous fusion-flicker threshold determination with well-defined acceleration of the frequency are the methods of choice. Since they have proved practically coincident and numerically higher than the others, they may be expected to afford the best reproducible reflection of the ability of the eye to fuse or to separate a sequence of light flashes.

The continuous flicker-fusion threshold determination may still be used in practice, however, if its shortcomings are recognized. These include, among other things, its failure to reflect the maximum fusion frequency, its greater dependence on the frequency acceleration, and the complicated adaptation conditions in the visual field during the threshold determination.

Comment: Studies on the critical frequency of flicker have been carried out for the last 100 years. As a matter of fact, the technique most used nowadays (that of keeping the stimulus intensity constant while the frequency of interruptions changes) is just 102 years old. It is generally felt that measurement of the so-called critical frequency of flicker offers valuable information about the condition and the purchasing of the visual apparatus. Still there is no instrument available for general clinical use and probably not even in the best equipped centers of clinical ophthalmic research will measurement of this magnitude be a routine test—unless some member of the staff might be personally interested in it. So far everyone doing research in this field has usually built his (or her) own instrument, used some personal technique of acceleration or deceleration of frequency, used his own intensity range, etc., and introduced some variable or variables which to him seemed to divulge *the* correct answer. For the general reader this all adds up to utter confusion. He finds in one paper that the critical frequency is greater in the periphery than in the centrum and (if he ever reads a second paper on the subject) he soon might find just the opposite reported. He will never know whether say, in amblyopia ex anopsia the critical frequency of flicker is increased or decreased in the foveal region, since he will find both reported. He will only be confused about the faculty of the eye to recognize the interruptions of stimulation (because this is what one actually is measuring) and the changes of this faculty in glaucoma, since reports are not consistent.

It is high time that somebody finally studied not "the critical frequency of flicker *in* . . . " or "the critical frequency of flicker *after* . . . " but "the critical frequency of flicker *under* . . . ," and here I mean under a variety of conditions of stimulation and of the simulated normal eye. Only after it becomes known under what conditions there is a meaningful difference between the light- and dark-adapted eye, the retinal centrum and periphery, etc., can one expect to get meaningful answers to the question of how critical frequency of flicker changes *in* glaucoma, *in* amblyopia, or *after* the application of some drug, poison, or therapeutic measure. The important investigations of Miles in glaucoma need to be continued, the method needs to be used, but first standard (not too expensive) instrumentation and a standard technique has to be developed.

With the author of the present study we finally have someone who has embarked on this worthwhile endeavor. This is already the second of his studies. He is trying to find out how critical frequency of flicker changes and what its actual values are if one starts with high interruption values and slows down until flicker is experienced, or starts with

low interruption value and increases frequency until sensory fusion occurs. He is trying to find out what the rate of acceleration or deceleration does to these values, whether it makes any difference if the subject is continuously exposed to the stimulus or only for brief periods, etc. It seems that by now he has found his method of choice. It is to be hoped that after this has been established, the much needed investigations of critical flicker frequency "in" and "after" will follow.

ARTHUR LINKSZ

Classics of Ophthalmology
JAMES E. LEBENSOHN, Editor

EXAMINATION OF THE VISUAL FIELD IN AMBLYOPIC DISEASE

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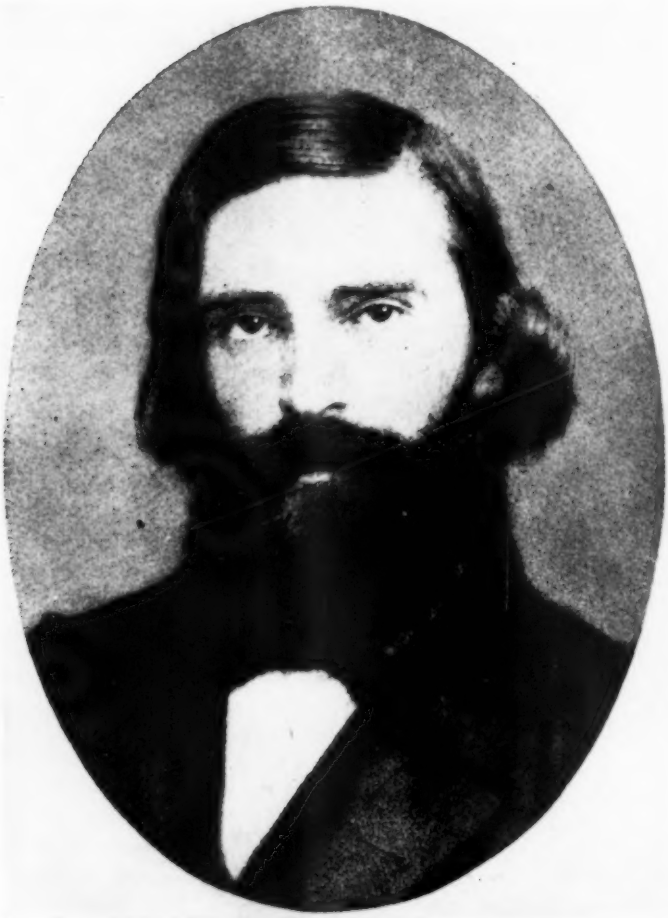
In determining central visual acuity, we are yet not at all informed concerning the patient's faculty of vision. The second and equally important part is the examination of the field of vision, or in other words the determination of the dimension and modality of eccentric vision. If this part of the examination were neglected, extensive visual disturbances of prognostic significance might be overlooked. A number of pathologic conditions are manifest for a time only by the changes in eccentric vision and it is only the last stage which induces progressive dimness of central vision. Even the patient's complaints may often remain to us unintelligible. Some patients who can read the finest print yet experience the greatest difficulty in walking abroad alone. In examining their eyes we find an almost complete intact central vision with a highly restricted eccentric vision. As an illustration I may demonstrate a subject who figures in the streets of Berlin as the blind musician, and who actually has to be led about, although he can distinguish letters (No. 4) of Jaeger's letter test. The opening of his visual space is about 10 degrees horizontal by 10 degrees vertical, in comparison to the normal of 174 degrees horizontal by 160 degrees vertical. To realize the situation of such a subject, we need but roll a sheet of paper into a tube which permits surveying at a 1½-foot distance an area of the above mentioned size in order to convince ourselves of the difficulty of orientation under such conditions. Though normally very eccentric impressions may be very indistinct yet they remind us of the presence of larger objects and induce us to confirm their presence by looking in their direction. If eccentric vision is interrupted, then every impression not exactly received in the axis of vision is missed and it becomes impossible to avoid obstacles in walking. Patients having a restricted field of vision frequently distinguish far objects better than near, and small better than large ones. This apparent mystery finds its quite natural explanation in the fact that large objects exceed the field of vision, but the image will fit into the small visual field only if the visual angle is sufficiently decreased. These conditions may be well illustrated by the above mentioned tube test.

No special method is required to determine the limits of the field of vision. For instance, we may mark any ocular object drawn on a board, if only we take care to have the axis of vision fixed immovably. We may then gradually displace any other ocular object from the direction of the axis of vision towards the limits of the field of vision by simultaneously performing slight lateral motions which will drive home the impressions. Finally, we mark the position in which this object becomes invisible. In order to guard against after-images and unreliable statements, we cause this object repeatedly to disappear and reappear in this position. At the most outward position from which reliable data is obtainable, we then mark definitely as the limiting position. The eccentric object should be large, well lighted, but not shiny or strongly reflective. I am not in favor of choosing a candle flame because the large diffusion of light makes it difficult for many test subjects to distinguish absolutely between the qualitative perception of the ocular object and the quantitative illumination which may be conducted by the sclera. Trial tests have convinced me that results fluctuate very widely when using candle light. It is also difficult to avoid disturbing reflexes due to the motions of the candle flame when the candle is already beyond the limits of the field of vision. Finally we must guard against after-images that will appear in the candle test even with highly peripheral impression.

In a highly restricted case the patient should be placed at a distance of several feet from a board with a fixed ocular object at the center. The surface of the board should be divided into many squares by two systems of vertical cross lines, and the squares should be numbered. While the patient fixes the central object we move a piece of chalk successively through the different squares towards the periphery of the board and note the number of the square in which the piece of chalk disappears. If this test is repeated in many directions it will give the exact shape of the field of vision, which may be marked on the board at the time or later. In order to infer from it the opening of the field of vision, it is but necessary to mark the distance of the eye from the board. For practical purposes I recommend adopting a standard for this distance. Most fields of vision observed in amblyopia were measured at the distance of 1½ feet.

We frequently observe patients whose field of vision is still extended and who yet manifest a remarkable clouding of eccentric impressions in certain directions. Usually this fact is brought to our attention because the patient is unable to find his way in spite of good visual acuity. It was first brought home to me while observing a patient whose unilateral blindness was due to glaucoma and whose other eye was in the unfortunate preliminary stage of periodical obscurations. Examination by the above described method during intervals when the patient could still read the finest print proved his field of vision to be of normal extent. But when I placed before him a sheet of paper and asked him to fix the central black spot, from which lines radiated in eight directions, every line bearing black spots at regular small distances, the pathologic condition of his eccentric vision was established by the fact that in certain directions he received distinct impression of numerous eccentric points, while in outward and upward



ALBRECHT VON GRAEFE

directions he did not. When I re-examined this patient at the onset of clouding—indicated by the onset of temporal pain—the restriction in eccentric vision had considerably increased and closely approached the center.

Our third consideration concerns the interruptions in the field of vision. Certain spots in the field of vision conduct none or very imperfect impressions in spite of no decrease in the extent of the field of vision nor in the clearness of eccentric impressions in certain retinal radials. The retinal portions involved may be wholly deprived of function, whereupon the phenomenon appears about like the normal blind-spot, that is, the patients do not perceive some dark shape, but at the spot in question they have absolutely no visual impression.

I have proved to my satisfaction that with smaller defects of this type and an otherwise normally functioning retina, a filling-in by superposition, a psychic process, occurs as in Mariotte's spot. Usually the retinal function is not completely paralyzed, but the retina retains a certain degree of sensibility to subjective and even to objective stimulation. Thus these interruptions will appear sometimes as light, sometimes as dark spots, conducting either no impression at all or enveloping the images seen in a cloud or a solar fog. These interruptions have extremely variable shapes, due to the basic causes of the disease. Often they appear as small round spots, which the patient may completely overlook because of their very eccentric position. They might even possibly be overlooked at examination, had not the ophthalmoscope indicated to us the study of a definite section of the field of vision.

In this respect there is one important disease which I must discuss in detail. We observe in the equatorial areas dark masses of pigment attached to the inner aspect of the choroid, radiating in starlike formation and often appearing like bone corpuscles. The intervals between these are free and almost bare of pigmentation, the large vessels actually appear so bare as to give the impression of a destroyed or atrophied choriocapillaris. This change, which is originally restricted to the equatorial sections, gradually progresses toward the posterior pole of the eye and simultaneously distinct symptoms of optic nerve atrophy present themselves. The optic papilla turns white and highly reflective, while the central vessels, and particularly the arteries, undergo progressive shrinking. Since this process starts in the equatorial sections, it results in progressive contraction of the visual field. I must again emphasize that in spite of marked changes in the optic nerve and in the central vessels, which constitute an essential part of the findings, the central vision may be preserved for a long time. No other disease presents in the majority of the cases such a disparity between visual acuteness and dimension of the visual field. As a rule the contraction is a regular concentric one, so the point of fixation remains exactly in the center of the visual field; yet sometimes this is not so. Judging by its course and the basic changes present, we cannot very well consider it an inflammatory process; the frequently occurring hereditary diathesis would also indicate other trophic changes.

The restrictions of the visual field in paralysis of the optic nerve due to central causes are likewise very interesting. In some cerebrospinal diseases we sometimes observe concentric contractions, which, however, never proceed as regularly as in the choroid disease just discussed. Usually the shape of the visual field becomes irregular and the point of fixation is as a rule eccentric. Often the shape of the visual field is absolutely identical in both eyes. Contractions in central diseases differ, moreover, from those in choriod disease just described, in that the central sight simultaneously depreciates considerably. Evidently this concentric contraction or restriction of the visual field corresponds to the gradual atrophy of the retina; the peripheral portions which are less highly innervated fading out first; here, too, the border of the visual field is not clearly defined, so that there is a certain transitional area within which retinal activity is de-

preciated to a minimum of quantitative perception. Ophthalmoscopic examination fails in such cases to detect any structural differences to mark off the border between the sensitive and the insensible portions. Usually only the general symptoms of atrophy of the optic nerve are apparent.

Particularly instructive for the physiology of the optic nerve are the hemianoptic restrictions in cerebral diseases. It happens not infrequently that in both eyes one-half of the visual field is wanting. There are numerous cases wherein the right eye has lost the right half of the visual field and in the left eye also the right; or vice versa, in both eyes the left half is wanting; while it is rather rare that the right half in the right eye and the left half in the left eye is wanting. The first kind of hemianopia is in itself far more disturbing to the patient; in the other, however, both visual field losses are compensated. How can we explain these extraordinary restrictions which occur with such great regularity? Retinal anesthesia beyond a vertical dividing line is observed as distinctly as in anesthesia starting at the meridian line after severing of the trigeminal nerve. Typical cases, moreover, experience no visual sensation whatever in the anesthetic portions. This can only be due to the distribution of the nerve elements. When we examine these cases more accurately and when we carefully consider all the other symptoms of the disease, we find that they apparently confirm the recent established theory of a semidecussation of the optic nerve. We learn that the symptom complex for the first (homonymous) type of hemianopia indicates a unilateral cerebral disease. For instance, if bilaterally the left half of the visual field is wanting, we observe frequent phenomena of left sided hemiplegia. If we assume this hemiplegia due to right sided cerebral disease causing paralysis and atrophy of the right optic stem, then we would satisfactorily explain this hemianopia by the statement that the right bundle of the paralyzed stem supplies the temporal section of the right retina, and the crossed bundle supplies the nasal side of the left retina. I am well aware that I am not stating anything new with this theory and its practical application; but as the matter is still so little known I feel impelled to communicate my observations concerning it, which I shall amplify in the future by corresponding autopsy findings. Let me now but briefly state that the simultaneous occurrence of the hemianopia described with its associated hemiplegia is not a rare finding, and I particularly urge the attention of hospital clinicians to it. The second (crossed) kind of hemianopia, in which both inner retinal halves are anesthetic, usually presents symptoms indicating a tumor or some pressure at the base of the cranium. If such a pressure is effective at the median line, then the crossed bundles (fasciculi cruciati—those close to the median line anterior as well as posterior to the chiasma) and thus the inner retinal halves will be especially involved. This kind of hemianopia never stops so sharply in the median line as does the other kind.

In diseases of the retina, retinitis apoplectica, degeneration of Bright's disease, various exudative processes, inequality of eccentric sight is still more frequent than actual restriction of the visual field and almost always associated with it. I have already mentioned that in retinal detachment indistinctness of eccentric vision occurs within an area adjoining the detached portions; also that excep-

tionally the detachment induces incomplete losses only and merely reduction of eccentric impressions to quantitative sensation. Granular exudations in the optic nerve are usually associated with the anomaly in question but as a rule, there is simultaneous intracranial disease which may possibly take a prominent part; at least as far as the ophthalmoscopically observed changes are concerned; with complete obscuring of the papilla, the visual field often shows not the least fluctuation.

It is really remarkable how many choroidal changes may be observed which are widely distributed throughout the eye-ground but with no portion of the visual field completely wanting. The interruption in posterior sclerotic choroiditis is particularly instructive. In this disease the conditions vary extraordinarily according to the stage and degree of the affection. In the beginning conduction is but slightly diminished in that part of the retina (largely) deprived of choroid. This may be on account of the excessive dazzling of this portion of the retina. It is then impossible to demonstrate by any means enlargement of the blind spot. Because of possible additional changes in the bared retina we may later on observe an enlargement of the blind spot which does not, however, correspond to the dimension of the white spot in the eye-ground, but is smaller. Extensive improvements in visual acuteness are rather frequently attained, even in prolonged and stationary affections; while changes in the visual field are but moderately attained and not at all in the majority of cases.

The prognosis in amaurotic affections with extremely depreciated central visual acuteness but perfect retinal conduction elsewhere is far better than in amaurotic affections with comparatively higher visual acuteness but severe anomalies of the visual field.

Editorial comment: Von Graefe's pioneer contributions to clinical perimetry were based on a simple apparatus comparable to the Peter hand campimeter. In his article on the glaucomas in 1869, he described in amazing detail the visual field in glaucoma simplex including the fingerlike defects about the blind spot and the nasal step. After the advent of Foerster's arc perimeter, von Graefe's method of campimetry fell into desuetude until revived by Bjerrum in 1889. Bjerrum added the conception of isopters and quantitative perimetry. The modern projection perimeters are ideally adapted to quantitative perimetry permitting a rapid diminution in the size and contrast of the test object and of the general illumination. In some cases even more delicate methods are required to reveal a reduction in sensitivity. The simplest of these is the exposure of two targets simultaneously on opposite sides of the fixation point and at equal distances from it. The inability to see then the target in the affected field is explained by gradients of excitability (Bender, 1952) or of visual attention (Allen, 1948). This phenomenon is observed in disturbances of the brain, but not of the optic nerve. Flicker fields are superior to standard perimetry in detecting regions of minimal depression including the central area in retrobulbar neuritis. Haitz utilized the Holmes stereoscope to maintain steady fixation. To extend the usuable field of the stereoscope, Lloyd developed the stereocampimeter.

When the media are cloudy, the field for color may be more reliable than that for white as color perimetry is less influenced by blurred images. Colored test objects are likewise useful in the central field as the presence of a 3 mm. red object is easier to determine than that of a 1 mm. white object. In 1953, Harrington introduced test objects of

sulfide inks rendered fluorescent by ultraviolet light. As these colors are of greater purity and saturation than those previously available, this innovation should give color perimetry a new impetus. The tachistoscopic device of Harrington and Flocks (1955) provides a satisfactory screening test that can be performed in a few seconds. This simplified test could well be included in the visual examination of motor vehicle drivers.

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Book Reviews

"Optics, the Science of Vision," by Vasco Ronchi; translated from the Italian and revised by Edward Rosen. (*New York University Press, 1957; $10.00.*) *It is reviewed here by Arthur Linksz who is the author of "Physiology of the Eye."*

Optics, the Science of Vision, by Vasco Ronchi, director of the National Institute of Optics in Arcetri, Italy, is a beautifully written, interesting, and yet disappointing book. Whether the excellence of its style has been translated (the word means "carrying on") from the original into English by Professor Rosen, a historian at City College, New York, or is the latter's achievement, this reviewer, unable to read the original, is in no position to tell. Certainly, the style is a paragon of clarity, reading the book is sheer pleasure and one of its chapters, "The Basis of Seventeenth Century Optics" (a review of the history of optics in 43 pages, from the predecessors of Aristotle to Kepler, Descartes and beyond) is more than worth the price of the book. But that is about as much as an ophthalmologist even moderately well grounded in physical, physiologic or geometric optics can expect to learn from this volume and the future ophthalmologist not yet familiar with these disciplines will find it a confusing and insufficient introduction with about ten pages devoted to the structure of the eye and the neurophysiologic events which lead to vision. Obviously, discussion of physiologic events preceding, and leading up to, vision is not the purpose of this volume of the science of vision. But, as it turns out, neither is geometric optics, and how and why the eye works as an optical instrument is left all but unmentioned.

A few quotations will but serve to show the author's purpose in presenting his material and the peculiar and particular point of view he wants to get across:

"For vision of the external world to take place, there must be a body emitting radiation which is propagated in the surrounding space, transmitted to the eye and absorbed by it. A stimulation . . . thus occurs, impulses are generated which . . . carry to the brain and mind not only the views that the radiation has arrived at the eye but also the characteristics of the stimulus."

This is all correct even if somewhat too general and popular but then we learn the following:

"*Then the mind goes into action.* It analyzes the information. . . . Having completed this operation, the mind portrays the conclusion with a model, or figure, an *effigy*. So too a sculptor, having received the description of an object by mail, studies it . . . and finally makes a clay model of it. The mind uses no clay, but constructs this non-material effigy *which it then places outside the body.* . . . Having finished this task, the mind confronts the luminous colored effigy and says that it 'sees the object. . . .' The complete sequence: emitting body,

emitted radiation, body receiving the radiation and re-emitting it, re-emitted radiation, optical system, eye, nervous system, mind, and finally effigy."

Again on another page:

"When all this information has been deduced it must be *represented*. For this purpose I attribute to the mind . . . the faculty of creating *effigies* /and/ the additional faculty of locating these effigies thus created at a suitable distance in the space before the eyes. When the mind has created the effigies and located them in front of the eyes, the ego says that it *sees the objects* of the external world."

Most of the rest of the book, some two hundred pages, is dedicated to the repeated and detailed promulgation of this strange doctrine as if no one would have ever proved the preposterous nature of all kind of projection theories or clarified the distinction between the physical space into which the objects and the eye are both imbedded and the spatial relations which we call subjective or sensual. With all this effort of explaining the location of "effigies," the actual optics of lenses, prisms and the eye is all kept on a disconcertingly primitive level and the illustrations are cluttered with unnecessary wave fronts, as if "waves" had greater "physical" reality or greater merit to explain the geometric optical part of vision than those "rays," the physical *ir*reality of which the author never tires to emphasize. Certainly, the geometric treatment of optical events is simpler, more fruitful, for any clinical purpose and more penetrating if this treatment avails itself of the fiction of rectilinear rays in the usual manner—in spite of the fact that a fiction they are. But so are wave fronts. And if it is a fiction that says, after refraction, wave fronts meet in some point it is no less a fiction that the refracted wave fronts are spherical and converge toward a point. The most satisfying fiction, as far as the practical imagination is concerned, is the fiction of particles, called "photons," traveling along Frajectorico, called "rays," and meeting, after refraction, in a sufficiently small area of the retina, called a "centric" by the author, although we might just as well continue to call it a "point." The accurate treatment of the actual events which lead to retinal (or other optical) image formation, in other words the treatment of so-called optical aberrations is complex enough if done in terms of rays. It becomes even more complex in the terminology of *wave* fronts and requires a mathematical apparatus which is way beyond the grasp of the average reader of this type of book. It is probably for this reason that the author constantly evades the issue of the actual form of refracted wave fronts and returns to the familiar ray language, when talking of caustic, spherical aberration, etc., at the same time constantly reassuring his readers that the "mind" doesn't bother about discovering that refracted wave fronts are actually hardly ever spherical.

Although this reviewer cannot help expressing the most vehement opposition to the whole philosophy of the author's presentation, he must confess that he was more than once fascinated by the elegance and simplicity of the sparingly and judiciously given mathematical formulas and that he picked many a sweet raisin from a loaf which, in general, was not to his taste. He found the "Appendix" in which the "Elements of Wave Motion" are treated quite rewarding

reading. But he was again and again aggravated by sentences as "The nerve impulses excite the mind to create a single point effigy where the two (ocular) axes intersect" as an explanation of binocular single vision and fusion, or: "If the observer fuses the effiges of the stick (the object he bifixates in the example given by the author) so as to see a single figure, he sees two pencils (the other object which in the given example the observer holds farther or nearer than the bifixated object) *and he sees nothing where the actual pencil* is" in the author's description of physiologic diplopia. All this, however, is topped by the following statement: "The retinas of the two eyes being sensibly symmetrical, a *correspondence* exists between the elements of one and those of the other. The mechanism of this . . . is not yet entirely clear. . . . In any case, *the correspondence is felt by the mind.*" Poor Helmholtz, Hering, Luneburg, Kohler, Ogle—they have all worked in vain. . . .

Ophthalmic Meetings

THE OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

The continents of Europe and America, the Commonwealth and some Iron Curtain countries were represented amongst a record gathering, when the 77th Annual Congress of the Ophthalmological Society of the United Kingdom was opened by the President of the Society, Mr. J. J. Healy in London on Thursday, April 11, 1957. The outstanding event in a most pleasant and satisfactory meeting was the presentation of the Bowman medal to Sir Stewart Duke-Elder, and his address on "The Aetiology of Chronic Glaucoma." This was only the third occasion since 1935 that the Bowman Lecture, the highest honor the Society can confer, has been awarded to a resident of Great Britain.

Sir Stewart did not disappoint his audience either in his choice of topic or its subject matter; on the contrary, some of the views which he expressed are quite likely to rekindle the flame of controversy that has from time to time surrounded this most fascinating and insidious of diseases. His statment that "the recent literature from Europe and the U. S. A., giving the impression that the angle and drainage channels are mainly at fault, is erroneous" and that the "primary cause is a vascular dyscrasia centrally determined, possibly by a center existing in the hypothalamus, producing a periodic vasotonia leading to structurai changes and eventually sclerosis," are unlikely to be accepted without question.

Sir Stewart also stated that there is as yet no conclusive evidence that the aqueous secretion has any effect on the intraocular pressure. The intraocular injection of Diamox, while inhibiting the carbonic anhydrase, does not lower the intraocular pressure; Diamox, therefore, has no effect on the aqueous secretory mechanism and possibly acts through an osmotic effect on the blood stream. A disturbance of the sympathetic and parasympathetic systems as evidenced by pupillary abnormalities and emotional instability may be seen in congestive glaucoma and diurnal variation in tension is demonstrable, even when the intraocular pressure has been successfully controlled by operation. In Sir Stewart's opinion the cupping of the optic disk is due to an interference in the blood supply to the optic nerve, the field defects pointing to a primary vascular lesion in the optic nerve, situated even as far back as the chiasma. The field changes are related more to the pallor than to the cupping; in the normal eye pressure for 4 minutes will lead to the commencement of an arcuate scotoma. In summing up, Sir Stewart said that great progress had been made within the last 10 years, but too much thought had been concentrated on the anterior part of the eye. He concluded his stimulating lecture by emphasizing a quotation from Bowman's talk to his students in 1951 of "the importance of the interdependence of the different systems and that no disease is a separate entity."

Following his address of welcome, Mr. Healy delivered an interesting paper on the "intraocular circulation in arteriosclerosis and high blood pressure."

After a brief resumé of the newer therapeutic measures, Mr. Healy urged greater liaison between the physician, the ophthalmologist and pathologist to speed the evolution of the emerging histopathologic pattern of hypertension.

Mr. Doggart opened a beautifully delivered talk on congenital cataract with the startling statement that 90 per cent of us had congenital lens changes, but added that 90 per cent of these were of no consequence. As regards the congenital ocular changes of rubella, he had never seen a case that did not show pigmentary changes in the fundus. Mr. A. B. Nutt dealt with the treatment and emphasized the fact that 6 or 7 points in management enunciated by Treacher Collins in 1908 still, in his opinion, held good. Mr. Nutt would defer operation in severe cases until the age of 6 months, since after that age the eye better tolerates operative interference. He stressed the danger of interference with the vitreous, particularly the possibility of perforating the posterior capsule in stirring up the lens matter. In bilateral cases he preferred to do both eyes as soon as possible after the age of 6 months.

Professor Franceschetti said that in the course of preliminary investigations on the subject in his clinic many cases appeared to have aminoaciduria; this was possibly associated with a kidney tubule deficiency. Sir Stewart Duke-Elder was of the opinion that this finding might be of tremendous importance and urged further investigation.

To open the afternoon proceedings of the first day, Mr. P. McG. Moffat and Mr. C. Dee Shepland spoke of intravitreal vitreous in retinal detachment surgery. Two eyes which had had a second injection of vitreous were lost because of panophthalmitis. Professor Paufique suggested that what he called 'lyophyllizated' or reconstructed, vitreous might contain substances that were not contained in aspirated fluid vitreous.

Mr. George Black followed with a description of his method of raising a scleral trap door for the application of diathermy to the choroid in retinal detachment work, thus reducing the destructive effect of the diathermy and ensuring a more constant coagulating effect.

With one of these technically near-perfect color films, Mr. H. B. Stallard demonstrated the advantages of the anterior approach for the shortening of the levator palpebrae superioris in the treatment of ptosis.

The final item in the first day's proceedings was a description by Professor Franceschetti of a simple instrument for taking lamellar grafts of constant thickness from the excised cornea.

The forenoon of the second day was taken up with a discussion on the "Ocular Aspects of Diabetes." Professor G. I. Scott from Edinburgh dealt with the ophthalmologic aspects and Dr. J. D. N. Nabarro gave the diabetic physician's approach to the problem. Dr. Nabarro agreed with the point of Joslin that strict control of the blood sugar level is definitely a deterrent to the development of retinopathy. He thought that a sustained high blood sugar level was more liable to cause damage than a swinging curve. Diabetic patients tolerated hypophysectomy poorly. Dr. Norman Ashton spoke with his usual authoritative brilliance on the "Experimental Aspects of Diabetic Micro-angiopathy;"

he discussed the significance of various experimental findings in relating diabetic retinopathy and glomerulosclerosis and their influence on future experiments.

Mr. E. S. Perkins expressed the hope that his paper on toxoplasmic uveitis showed that the condition existed as a distinct entity and produced convincing figures in support of the contention that Daraprim was of definite benefit in the treatment of the condition.

Dr. Frank Law described a case of lacrimal obstruction cured spontaneously with the removal of the patient's appendix. An unusual case of Marcus Gunn syndrome was pictorially demonstrated by Mr. Rupert Parry and a case of rupture of the liver with the typical ocular changes was described by Mr. G. T. W. Cashell.

A stimulating discussion on the association of secondary glaucoma with lens changes was precipitated by the description of the histologic findings in 3 cases of phacolytic glaucoma by Dr. Patrick Schofield; the distinction between this condition and the phacoanaphylactic, phacotoxic and phacogenetic reactions was admirably discussed by Mr. A. J. Leigh.

Sir Stewart Duke-Elder's memorable lecture ended this day's proceedings.

The final session of the meeting on Saturday, commenced with a paper by Mr. J. H. Dobree on venous obstruction at the disk in chronic glaucoma. The author pointed out that central vein thrombosis, venous coils, anastomotic vessels, and hemorrhages at the disk edge would appear to be the result of the glaucomatous cupping.

A foreign body detector and locator capable of discriminating between magnetic and nonmagnetic fragments, even of a size less than 1 cu. mm., was described by Mr. M. J. Roper-Hall; it was pointed out, however, that the instrument would not be of assistance where foreign bodies of glass and stone were concerned. During operations the adjustments for temperature drifts could be made as easily as managing a diathermy machine.

Mr. John Ellison described a case of retinoblastoma with unusual postmortem findings, and Mr. Joseph Minton in a talk on uveitis in childhood described the occurrence of a band-shaped keratopathy 4 years before the onset of the articular changes of Still's disease.

Dr. F. R. Rodger in a talk on the pathogenesis of ocular onchocerciasis stated that experimental work on animals had shown conclusively that it was the dead parasite that led to the inflammatory reaction and that nearly all the manifestations of human ocular onchocerciasis were reproduced in the rabbit. It is postulated that a toxin secreted by the free adult worm may lead to posterior segment lesions, particularly choroidoretinal degeneration.

An investigation into the role of various viruses in the production of conjunctivitis and keratoconjunctivitis in cases presenting with conjunctival inflammation at Moorfields in 1956 was described by Mr. Barrie R. Jones *et al.*; the present day pattern of conjunctivitis and some points in the differential diagnosis were discussed.

This ended a very successful and pleasant meeting!

F. D. McAuley
Dublin

COMBINED MEETING OF THE IRISH OPHTHALMOLOGICAL SOCIETY AND THE SOCIETY OF BRITISH NEUROLOGICAL SURGEONS

For its 36th Annual Meeting held in Dublin on May 16th, 17th and 18th 1957, the Irish Ophthalmological Society invited the Society of British Neurological Surgeons to present jointly a program of common interest. The Joint Presidents were Dr. Alan Mooney (I.O.S.) and Mr. W. R. Henderson (S.B.N.S.). A number of visitors from the United States as well as many from Europe and the Commonwealth were present for a very interesting series of lectures and discussions. This was the first occasion that the Society of British Neurological Surgeons, the second oldest in existence—having been founded six years after its American counterpart—had its Annual Meeting in conjunction with the Society of another speciality. On the eve of the Meeting Dr. L. B. Somerville-Large the energetic Secretary of the Irish Ophthalmological Society, gave a cocktail party to the members and guests of both Societies at his beautiful riverside home outside Dublin.

To the distinguished list of Montgomery Lecturers comes another of International renown in Dr. Frank B. Walsh from the Wilmer Institute of Johns Hopkins Hospital; he delivered a paper entitled "Third Nerve Regeneration; Clinical Evaluation." Dr. Walsh from his vast wealth of clinical experience demonstrated the phenomenon of misdirection and as an analogy described the mass contraction of muscles innervated by the 7th nerve in an effort to perform some muscular function supplied by one of its branches. In the regeneration of a third nerve paralyzed by injury or by the pressure of an aneurysm, adduction of the eye may cause elevation of the eyelid whereas abduction leads to lowering of the lid; elevation and depression of the globe are inhibited. Palsies associated with migraine and diabetes tend to clear up completely without misdirection.

Dr. Alan Mooney in his Presidential Address discussed some neuro-ophthalmological problems. He emphasized the importance and the relative simplicity of percutaneous arteriography. In reference to the sequelae of tuberculosis meningitis, he pointed to the value of a timely ventriculostomy as a sight-saving procedure and showed that visual recovery may continue for over 12 months. The President's display of arteriograms was full testimony to the excellent work performed in the neurosurgical unit in Dublin's Richmond Hospital with Dr. Mooney's invaluable assistance.

Dr. Max Chamlin from New York started a lively discussion by his paper on "Visual Field Changes produced by X-ray treatment of Pituitary Tumors." He impressed upon his audience the necessity of giving the patient plenty of time to read the visual acuity chart as otherwise an inaccurate guide to the post-irradiation progress of the patient might emerge.

Professor Krayenbuhl (Zurich) in a paper entitled "The Diagnostic Value of Orbital Angiography" mentioned that the injection of a 60 per cent contrast

medium into the carotid artery would lead to visualization of the ophthalmic artery in 98 per cent of cases. He described an interesting method of injecting the facial vein with the contrast substance.

Dr. Uihlein from the Mayo Clinic discussed acute visual failure as a neurosurgical emergency. He described the saving of vision by prompt surgery in a patient who sustained a hemorrhage into a pituitary tumor, and the employment of needless surgery in another patient who eventually turned out to have had toxic amaurosis from the use of a benzene spray. He favored the old axiom that one look was better than a hundred guesses.

The main subject for discussion at the meeting, "The Blood Supply of the Chiasma and the Optic Nerve in relation to Visual Field Defects," occupied the afternoon of the first day. The first of the opening speakers was Professor François from Ghent who demonstrated to an appreciative audience the results of his well-known investigations into the vascular supply of this area of the brain. Professor Brodie Hughes (Birmingham, England) spoke of the difficulty of explaining the occurrence of a sharply delineated field defect which often occurs after exsanguination resulting from a gastrointestinal hemorrhage.

Between the two previous speakers Dr. Erskine, Professor of Anatomy at Trinity College, Dublin, produced a fascinating display of photographs using color with a phase-contrast microscope to demonstrate the glial tissue of the optic pathway; he showed that the glial system had a dynamic function and did not only subserve the purpose of a supporting mechanism.

In the subsequent discussion Sir Stewart Duke-Elder inquired from Professor Erskine "if, in view of the green color of his photographs, the new microscope was indigenous to Ireland." In reply Professor Erskine pointed out that the instrument had been produced only a few months ago by one of the leading German Optical Instrument makers, and that this was the first occasion it had been used for such an investigation.

A reception by Dr. Alan Mooney was held prior to the combined Dinner of both Societies at the Gresham Hotel on the evening of the first day. During the evening a presentation of a silver salver was made by the Society of Neurological Surgeons to Mr. Adams McConnell from the Richmond Hospital in appreciation of his services to the Society, of which he was one of the founder members; it was mainly due to his efforts that the Annual Meeting had been held more often in Dublin than in any other city with the exception of London and Manchester.

The program for the second day commenced with the examination and discussion of clinical cases in the Royal Victoria Eye and Ear Hospital. Messrs. Arthur Guinness, whose brewery is one of the largest in existence, were hosts at luncheon to the members and guests of both Societies; an excellent lunch it was, and when all the participants could be mustered together it required a police escort of 21 motor cycles to conduct the party to Trinity College for the afternoon session.

Mr. J. Roper-Hall from Birmingham discussed various causes of optic disc edema without raised intracranial pressure; he mentioned that four out of five cases had local vascular disturbances at the optic disc. The normal arteriovenous ratio is 3:1; if it falls to 3:2 edema results. Mr. Adams McConnell pointed out

that often on trephining the skull of a patient in whom the lumbar pressure of the cerebrospinal fluid has been found to be normal the brain will ooze out and appear edematous. Mr. Dixon Wright felt that factors other than raised intracranial pressure, such as anesthesia, could account for this.

Professor Scott from Edinburgh discussed the ocular aspects of endrocine exophthalmos. He was of the opinion that the lid retraction in thyrotoxic exophthalmos had a day to day variation and responded to prostigmine. In malignant exophthalmos lid retraction does not exist without defective elevation.

Dr. Frank B. Walsh's Montgomery Lecture concluded the day's scientific proceedings.

A reception by the Minister for Health and Mrs. McEntee in the evening preceded a Dinner given by An Bord Failte (The Tourist Board) at the Royal Hibernian Hotel.

On the final day the two Societies had separate programs. The Ophthalmological final session commenced with a paper on the Detection of Glaucoma by Dr. T. J. McDougald (Dublin) who discussed the methods practiced in the various clinics on the continent of Europe.

In the discussion which followed Sir Stewart Duke-Elder spoke of the value of the water drinking test and the bulbar pressure test. He mentioned that at the Institute of Ophthalmology in London a suction cup was being used now instead of bulbar pressure.

Mr. Stallard presented a film of his operation of anterior flap sclerectomy with basal iridectomy. He was succeeded by Sir Luigi Preziosi from Malta who spoke on the flap and filtration in Preziosi's operation for glaucoma.

The final item was a paper on the Technique and Results of Retinal Detachment Surgery using Binocular Indirect Ophthalmoscopy by F. D. McAuley (Dublin). The 'American Optical' Binocular instrument and the new British instrument made by Hamblin were on show.

To conclude a very happy meeting, during the course of which the wives of the visitors were taken on sight-seeing tours by the wives of the local doctors and other volunteers, Mr. and Mrs. Adams McConnell entertained members and guests at tea and sherry at their home on Saturday afternoon and evening.

F. D. McAuley
Dublin

UNITED STATES SPRING MEETINGS 1957

The remarkable total of 78 papers was presented to unusually large and interested audiences at the annual meetings of the American Ophthalmological Society, the Section on Ophthalmology of the American Medical Association and the Association for Research in Ophthalmology. Nearly every paper was followed by an assigned, prepared and competent discussant so that at the end of the meetings one had been presented with an almost overwhelming mass of data, charts, kodachromes, triumphs, tragedies, and the other ingredients which make for lively medical gatherings.

The 93rd annual meeting of the American Ophthalmological Society was held at the Homestead, Hot Springs, Virginia, May 30, 31, and June 1, 1957. One

hundred and thirty five members and twenty three guests attended the three one-half day sessions over which Frederick C. Cordes presided. Nineteen papers of broad interest were presented and, as always, the exchange of ideas and experience made the discussions which followed unusually interesting. Robert Shaffer indicated the value of gonioscopy as an operating room procedure in which following paracentesis the anterior chamber is deepened with saline in the angle closure types of glaucoma to learn if the angle is open so that peripheral iridectomy would be effective. If the angle is nearly closed by goniosynechiae Chandler's goniotomy or a cyclodialysis is indicated. C. Wilbur Rucker, basing his historical study on Sir Isaac Newton's fifteenth query appended to "Opticks," which concerns the semi-decussation of the optic nerves at the chiasm, presented a charming and delightfully illustrated inquiry into Newton and his times. The meetings were never so long that they became tedious; the weather was fair; the ladies lovely; the golf, tennis, skeet, fishing, riding and visiting pleasant, and the meeting was most enjoyable.

The Howe Medal was awarded to Georgiana Dvorak-Theobald, a selection which met with enthusiastic and prolonged applause. Henry Wagener, Chairman of the Committee on Prizes, presented the medal with a carefully documented and lightly sentimental resumé of Dr. Georgiana's contributions to teaching, research, pathology, the American Board, and to meetings and discussions.

Walter S. Atkinson of Watertown, New York, was elected president and Derrick Vail of Chicago, Illinois, vice-president for 1958. Maynard C. Wheeler was re-elected secretary-treasurer and Gordon M. Bruce, editor of the Transactions. The next meeting of the society will be held at the Greenbrier, White Sulphur Springs, May 29, 30, and 31, 1958.

The Association for Research in Ophthalmology meeting dominated the joint session held in conjunction with the Section on Ophthalmology of the American Medical Association. Even with the heartless exclusion of excellent topics the final program totalled 40 papers, some highly specialized and of limited interest, but others of broad clinical application. Surprisingly, even the sessions dealing with unusually erudite and complex studies were well attended and made evident that a vigorous, original and provocative group of investigators is emerging in American ophthalmology. Two hundred and eighty five registered for the sessions.

The first Friedenwald Memorial Lecture was given by Dr. John E. Harris of the University of Oregon, who spoke on the "Physiologic Control of Corneal Hydration." The Proctor Medal recipient was Dr. Norman Ashton of England who spoke on "Ocular Vascularization in Health and Disease." The studies on retrolental fibroplasia in time may indicate the cause of diabetic retinopathy and studies concerning the role of hypoxia and neovascularization are being directed in that direction. At the annual banquet, Ashton's remarks concerning the honor of being the Proctor Medal recipient—preparation of a biography, a bibliography, a photograph, a light talk for the banquet, an erudite lecture for the scientific session and an unforgettable discussion of the preparation of the paper on hepatectomy—set a serio-comic standard for years to come.

It was obvious that the Association for Research program is rapidly outgrow-

ing the joint meeting with the Section and plans were presented for an interim meeting in January to reduce the large number of papers at the June meeting.

Theodore E. Sanders of St. Louis, Missouri, Chairman of the Association for Research, arranged an extraordinarily interesting meeting which, despite the number of papers read, adhered to the time schedule most exactly. He will be succeeded by Michael J. Hogan of San Francisco, California; Alson E. Braley of Iowa City, Iowa, was elected a new trustee and Lorand V. Johnson of Cleveland, Ohio, was re-elected secretary-treasurer.

The Section on Ophthalmology of the American Medical Association sessions, under the leadership of the Chairman, Algernon B. Reese, were outstanding. Professor Jules François of Ghent, an invited foreign guest, spoke on the "Differential Diagnosis of Tapeto-Retinal Degeneration" in an extraordinarily competent and comprehensive manner. Frank W. Law of London, spoke on "Iridencleisis in Buphthalmos" with that lightness, erudition, and excellence which seem to characterize all ophthalmic visitors from the British Isles.

The business meeting of the Section was much more routine than has been customary the past decade, due largely to the interpretation of the constitution and by-laws of the American Medical Association that the purpose of the various sections is to present forums on the scientific aspects of medical practice. All other aspects, social, political, and economic, are within the purview of the House of Delegates of the Association. However, thanks largely to the vigorous representation by Harold G. Scheie, secretary of the Section, and other officers, the Section will be permitted to carry on liaison activities with committees of other national ophthalmic groups. The oral report of the representative to the American Board of Ophthalmology acknowledged the many valuable expressions of opinion received concerning the establishment of a Board of Ophthalmic Surgery and announced that plans for establishment of such a board had been discontinued.

A group of fourteen ophthalmic exhibits was presented. The Section prize of $250 was presented to David Volk, Western Reserve University School of Medicine, for the exhibit, "Conoid Ophthalmic Lenses: An Original Development in Subnormal Vision Aids." This exhibit received a certificate of merit as well as the exhibit "Cancerous and Pre-cancerous Melanosis of the Conjunctiva" by Algernon B. Reese and Bradley R. Straatsma, of Institute of Ophthalmology of Presbyterian Hospital and Columbia University College of Physicians and Surgeons, New York. Visual acuity, Harrington visual field screening and the intraocular pressure were recorded in over 500 physicians by the National Society for the Prevention of Blindness in an exhibit directed toward annual physical examinations sponsored by the American Academy of General Practice. The Section prize of $250 for the best paper presented at this meeting was awarded to Dr. James E. Bennett and Arby L. Bailey of Cleveland for their paper, "A Surgical Approach to Total Xerophthalmia Through Transplantation of the Parotid Duct."

The Gold Medal of the Section for Service to Ophthalmology was awarded to Dr. William L. Benedict of Rochester, Minnesota, who has participated in almost every phase of ophthalmology and contributed enormously of his energy

and talents to education, administration, and leadership in ophthalmology. Officers of the Section for 1958 are: Chairman, Dohrmann K. Pischel, San Francisco, California, to succeed Algernon B. Reese, and Vice-Chairman, Ralph W. Danielson, Denver, Colorado, to succeed Hedwig Kuhn. Harold G. Scheie continues as secretary and Ralph O. Rychener as delegate to the House of Delegates with Harvey Thorpe as alternate. Frank W. Newell continues as the Section representative to the Committee on Scientific Exhibit.

The Herman Knapp Medal, which was awarded in 1953 to Charles K. W. Asher for his paper on "Aqueous Veins" and prior to that in 1939 to Frederick C. Davis for his paper on "Primary Tumors of the Optic Nerve" was awarded to Goodwin M. Breinin of the New York University Postgraduate School of Medicine for his paper read in 1955, "The Nature of Vergence Revealed by Electromyography." Dr. Breinin has opened a new method of approach to the nature of ocular muscle innervation, developed a valuable method of diagnosis and well deserved the recognition for his contribution to fundamental and clinical research.

The final day of the meeting was featured by an unusually interesting series of papers on cataract extraction. The operation continues to excite the same interest in the ophthalmologist that "Hamlet" does in the actor, and the session was unusually well attended.

The next meeting of the Section and the Association for Research will be in San Francisco in June, 1958.

FRANK W. NEWELL

Current Review

GONIOSCOPY

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Gonioscopy may be defined as biomicroscopy of the anterior chamber angle. Although this method of examination is well known, it is not used as universally as is desirable. Furthermore, some of those who use it may be misled by anatomic and congenital variations in topography. The purpose of this review is to summarize gonioscopic anatomy and to point out the diagnostic and therapeutic advantages to be gained by accurate gonioscopic examination.

GONIOSCOPIC METHODS

The three most widely used contact lenses for gonioscopy are the Goldmann, the Allen-Thorpe, and the Koeppe. The first two are used in conjunction with the slit lamp and hence need no extra equipment for magnification and illumination. It is the opinion of the authors that with proper magnification and lighting the Koeppe lens gives a clearer angle picture. Furthermore, it is the only one which may be used in surgery for examination and for goniotomy. Consequently, only the Koeppe lens* will be discussed in this paper.

The best light to be used with the Koeppe lens is the Barkan hand illuminator. For magnification a stripped down version of the Haag-Streit (Goldmann) microscope is light enough to be held steadily by hand. It gives 10 × magnification. The Koeppe lens itself magnifies 1.5 ×, giving a total of 15 ×. Total magnifications in excess of this 15 × require the use of either a Barkan stand or a telescopic microscope support to permit steady focus on the angle structures.

TECHNIQUE OF INSERTION

The patient should be lying comfortably supine with the head turned toward the examiner and the eyes looking at the examiner's nose. The Koeppe lens is held in the examiner's right hand for the right eye and in the left hand for the left eye. It is held at the equator by the thumb and middle finger. The upper pole of the lens is pivoted outward so that the upper eye lashes cannot be touched. The examiner holds his head so that the patient has to look slightly upward to see the examiner's nose. The lower pole of the lens is then inserted and pushed down against the lower lid, which has been held away from the eye by the opposite hand. The examiner moves his head caudad (that is, toward the patient's feet) so that the patient moves his eyes downward, releases the patient's lower lid, and pulls the upper lid away from the eye. The upper pole of the lens is then pivoted

* The 16-mm. Koeppe lens is the most useful size.

against the eye and the upper lid is released. Still holding the lens equator in line with the palpebral aperture, the examiner's fingers now lift the nasal edge of the lens well away from the eye while the other hand fills the space between the lens and the eye with physiologic saline from a wash bottle or an eye dropper. Introduction of 0.2 cc. of solution will fill the lens cup. The index finger now drops down onto the dimple on top of the contact lens and pushes straight back toward the pupil. This displaces excess saline and prevents ingress of bubbles. While the examiner holds the lens with the index finger, the patient's head is now turned straight, the examiner's head coming up with the patient to keep the eyes straight. An assistant can now steady the lens with the muscle hook while gonioscopy proceeds.

EXAMINATION OF THE ANGLE

(*a*) *Pupil and Iris.* It is best to start gonioscopy by looking at the pupil to obtain rapid intraocular orientation. The anterior lens surface should be observed for glaukomflecken and for posterior synechias. This is also one of the best positions in which to see the white dandruff-like flecks on the posterior iris which are diagnostic of capsular exfoliation. The examiner's gaze should then pass over the plane of the iris, noting its flatness, which usually denotes a deep anterior chamber, or its convexity, which is seen with a shallow chamber. Neovascularity, hypoplasia of the iris, polycoria, or iridodonesis should be noted. The final iris roll (Fig. 1, *1*) can be seen at the beginning of the angle recess. This roll is just central to the thin spot in the iris at its point of union with the ciliary body.

(*b*) *Ciliary Body—Iris Processes.* Beyond the final iris roll one drops back into the angle recess (Fig. 1, *2*). At birth this recess has not yet developed. In the adult the recess is formed by the concave anterior surface of the ciliary body. The anterior iris stroma is continuous with the surface and wraps around it, running up to Schwalbe's line as the uveal meshwork. It is usually unpigmented above the scleral spur. The vestigeal pectinate ligament of iris processes (*3*) form thickenings in this tissue or may completely bridge the angle recess, terminating at or even

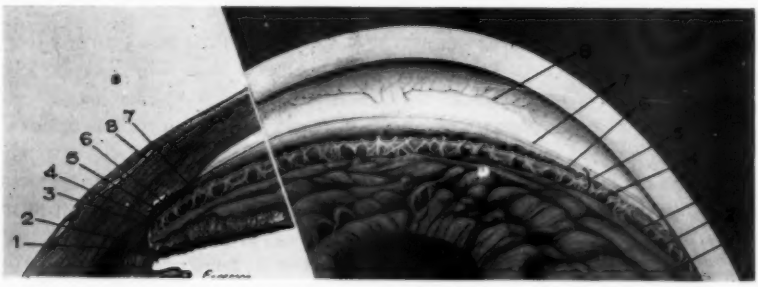

FIGURE 1. Composite microscopic and gonioscopic drawing of normal angle structures. (*1*) Last iris roll; (*2*) angle recess and ciliary body band; (*3*) iris processes; (*4*) scleral spur; (*5*) trabecular meshwork; (*6*) Schlemm's canal-trabecular meshwork band; (*7*) Schwalbe's line; (*8*) limbal blood vessels.

above the scleral spur (*4*). The less completely differentiated angles have more iris processes, and in instances of incomplete embryologic cleavage of iris from cornea these processes may run completely up to Schwalbe's line. The full-blown picture of this condition is seen in Axenfeld's syndrome, or posterior embryotoxon, which will be discussed under congenital glaucoma.

Usually the iris processes run only as high as the spur. Some are single, others branched. In blue eyes they are light gray in color and can be seen with difficulty, but in brown eyes the pigmented processes stand out prominently against the light background of the scleral spur. In eyes with a deep recess into the ciliary body it is possible to mistake these processes as synechias covering the angle wall. True synechias are formed when peripheral iris becomes attached to the trabecular wall. There are several clues which are used to distinguish iris processes from peripheral anterior synechias. The synechias tend to be much broader. Iris processes wrap around the angle recess, following closely the contour of the concavity of the ciliary body in that area. With peripheral anterior synechias the angle recess is obliterated by attachment of the iris directly to the anterior angle wall. If the angle landmarks and the angle recess are seen clearly in one area, whereas immediately adjacent to it these landmarks are blocked by attachment of the iris to the anterior angle wall, a peripheral anterior synechia is present. If iris rests against the trabeculum for any reason, synechias of a brown iris form more easily and are more solid than those formed by a blue iris.

(*c*) *Scleral Spur.* In wide angled eyes the spur (Fig. 1, *4*) is easily seen as a gray-white line at the anterior insertion point of the ciliary body. If it can be seen, one knows that any obstruction to outflow lies in the trabeculum (*5*), Schlemm's canal (*6*), or the aqueous veins rather than in synechias or angle closure by iris approximation. The spur is the point of termination of the corneoscleral trabeculum.

(*d*) *Trabeculum and Schwalbe's Line.* In practically all eyes the end of Descemet's membrane and the beginning of the trabeculum, which is known as Schwalbe's line (Fig. 1, *7*), can be seen by slit lamp as a hazy zone on the inner surface of the peripheral cornea (Burian and Allen). Seen through a contact lens, Schwalbe's line varies considerably in appearance in different eyes. It may be seen as a marked white or translucent ledge projecting into the anterior chamber, or it may be only a vague line of demarcation between the smooth inner cornea and the less transparent rough texture of the trabeculum. It is considerably higher on the angle wall than the neophyte expects and the microscope must be held quite low, with the line of vision skimming the surface of the iris, to get proper visualization. It is at Schwalbe's line that the change in radius of curvature occurs between the corneal curve and the scleral curve. This change in curvature and the beginning roughness of the trabecular wall at the end of Descemet's membrane give a lodging place for pigment granules which have been carried by the aqueous convection currents. These pigment dots tend to deposit at Schwalbe's line, especially in the lower angle. If a slit lamp beam is used with the Allen or Goldmann lens, the inner and outer lines of the corneal parallelepiped come together at this point. All these factors should be used in identifying this important landmark.

Between Schwalbe's line and the spur extend the fibers of the trabeculum. The innermost fibers, known as the uveal portion, run past the spur, some into the ciliary muscle and the rest in a thin layer continuous with the anterior iris stroma. In the posterior half of the corneoscleral trabeculum, anterior to the spur, lies the filtering portion of the trabeculum in front of Schlemm's canal. It frequently is marked by a light gray or brown band. In diseased or aging eyes, more and more floating pigment is sifted out of the aqueous as it filters through the trabeculum. This deposition of pigment results in the trabecular pigment band, which is the most valuable landmark in the angle because it shows the point of aqueous outflow from the eye. In normal eyes a pink band can sometimes be seen at this position. This is blood which has regurgitated into Schlemm's canal as a result of pressure exerted by the contact lens. It is seen more commonly in persons under the age of 50. Blood also enters the canal if there is any increase in venous pressure, as by jugular vein compression or with the vascular engorgement of inflammation. It is rare to find blood in Schlemm's canal in simple glaucoma.

CHANGES WITH AGE

The two striking features of the infant angle are absence of an angle recess and translucency of the tissues. The anterior iris stroma tends to be poorly developed, allowing the posterior pigment layer to be seen. The iris inserts on the anterior edge of the ciliary body, but the excavation of the ciliary body which results in the angle recess in the adult is usually not present. The trabecular wall has no pigment band and is amazingly translucent. Its surface glistens with the shagreen of stippled cellophane. The young adult usually has not developed a trabecular pigment band, but tissue translucency has decreased. This change continues into old age. The trabeculum gradually becomes more opaquely white and picks up more pigment, especially in the lower angle. Intraocular disease, such as iritis or glaucoma, usually results in an increase in this pigmentation.

EMBRYOLOGY OF THE ANGLE

In the 65-mm. embryo (11–12 weeks) most of the adult structures are recognizable except the circular fibers of the ciliary muscle. Schlemm's canal is at a level with the bottom of the angle. In the last 20 years Ida Mann's theory of the resorption of embryonic tissue to achieve the adult relationship has been in vogue. More recently the theory of Treacher Collins has been revived, particularly by Burian and Maumenee, who believe the angle forms by a relative overgrowth of the corneoscleral portions with resultant splitting of the iridic portion from the cornea. Iris processes are the result of incomplete cleavage. This cleavage extends down into the anterior ciliary body beyond the spur, giving rise to the angle recess.

CLASSIFICATION

The grading of angle width is aimed at differentiating an angle that is closed from one that is open. There is further distinction between an angle that is widely open and one that is narrowed and, therefore, predisposed to sudden closure. An

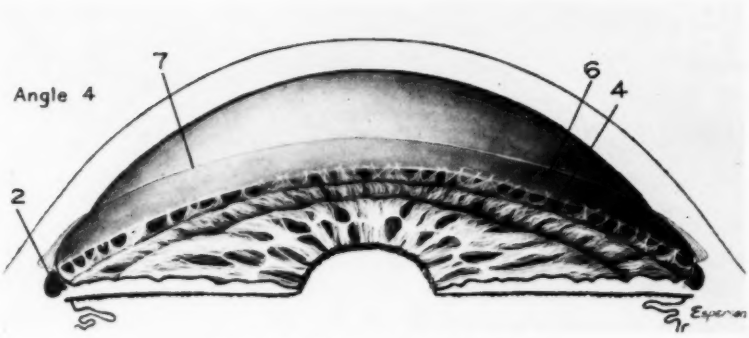

FIGURE 2. Widely open angle, grade 4

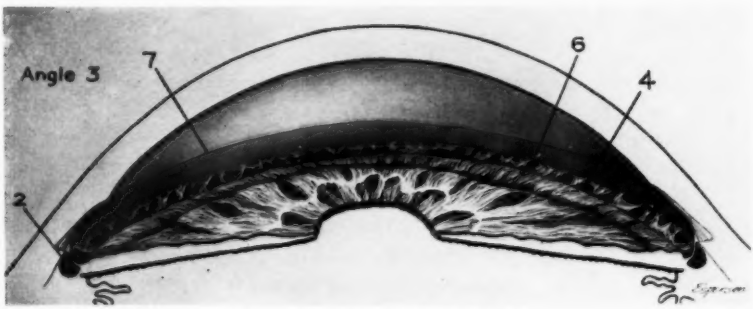

FIGURE 3. Open angle, grade 3

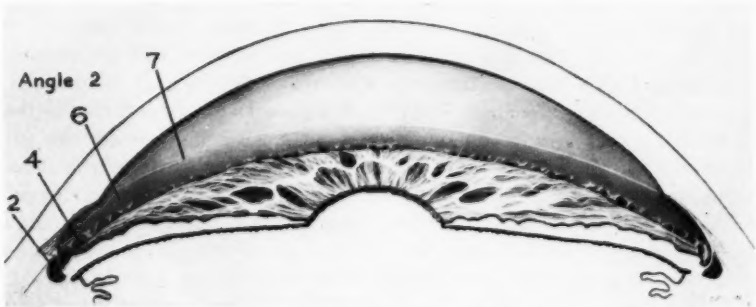

FIGURE 4. Open angle, grade 2

important aspect of this classification is in alerting the examiner to the possibility of angle closure in a narrow angle eye. Angle width is graded from 0 to 4. A grade 4 angle (Fig. 2) is found in a deep chambered eye with a flat iris plane such as is typically seen in the aphakic eye. The angle is wide open with all the landmarks

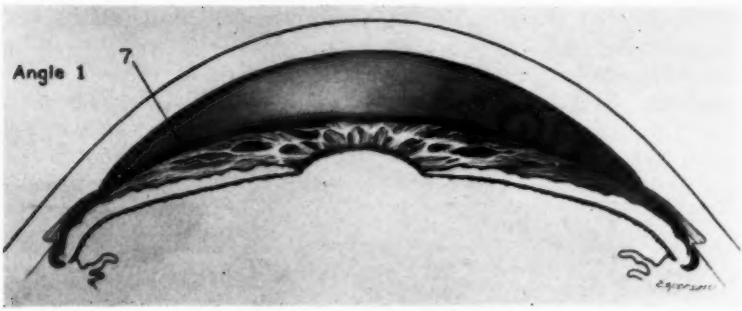

FIGURE 5. Open angle, grade 1

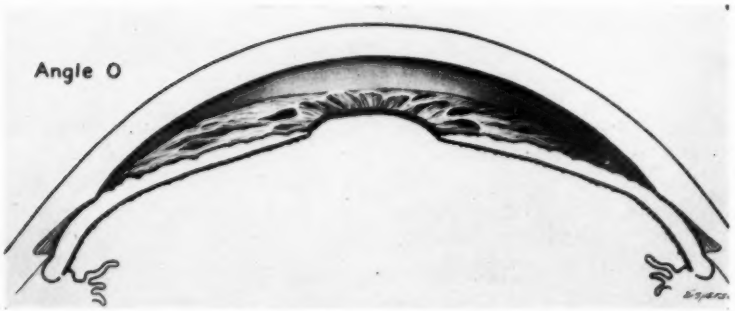

FIGURE 6. Closed angle, grade 0

easily visible gonioscopically, with the iris well separated from the angle wall. A grade 3 angle (Fig. 3) is also wide open but not quite to the same extent as grade 4; this width of angle is generally found in most normal eyes of young adults. Grade 2 (Fig. 4) is still an open angle, but not quite as wide as grade 3, the iris being a little closer to the angle wall. However, the angle landmarks are still visible, including the ciliary body band. Grade 1 (Fig. 5) is a narrow angle, with the iris quite close to the angle wall and generally obscuring the ciliary body band and even the scleral spur but leaving the trabecular pigment band, the filtering area itself, visible. In order to sight over the last iris roll in this condition it is necessary to elevate the angle of observation so that one sights obliquely down just under Schwalbe's line. A grade 0 angle (Fig. 6) is closed by apposition of the iris up to and, occasionally, even beyond the level of Schwalbe's line. If there seems to be a separation between iris and angle wall but the examiner cannot be sure of angle patency, such an angle is called a "slit."

Angles graded 0, slit, or 1 are susceptible to the development of acute angle closure glaucoma. This may even be precipitated by pupillary dilatation in the office. Grades 3 and 4 will never develop an attack of acute angle closure glaucoma and these pupils may be dilated in the office with impunity. Grade 2 is unlikely to result in acute angle closure glaucoma. However, with increasing age, increasing

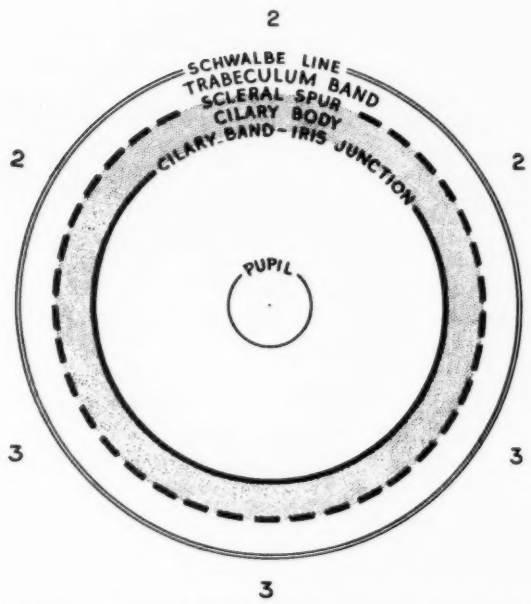

FIGURE 7. Diagrammatic representation of angle structures showing method of grading angle width.

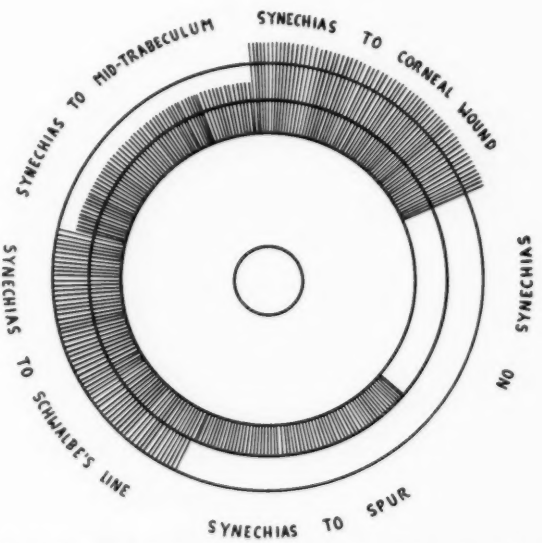

FIGURE 8. Method of using angle diagram to illustrate extent of synechias.

lens size, and in some instances a trend toward physiologic pupillary block, the angle tends to become narrower. Thus a grade 2 angle at age 40 may become a grade 1 at age 50 and then develop an attack of acute glaucoma. There is a normal variation in angle width in various portions of the same eye. The upper angle is usually narrower, due to the normal forward position of the upper pole of the lens. An angle which grades 1 above will usually be at least a grade 2 below. For this reason angle width is usually numbered on the angle diagram as shown in Figure 7. It is also used to diagram the position and extent of lesions in the angle. Diagramming of synechias is shown in Figure 8.

ANGLE CLOSURE GLAUCOMA

If one were to select the most important single diagnosis to be made by gonioscopy it would be that of a narrow angle. It is this type of angle that predisposes a patient to an attack of acute angle closure glaucoma. The knowledge that a narrow angle is present enables the ophthalmologist not only properly to interpret the patient's previous symptoms of periodic blurred visual acuity, halos, and headaches, but also to be alerted to the possibility of this patient's suffering an attack of acute glaucoma in the future. The converse is also of value. For instance, if a patient complains of morning headaches and perhaps a mild decrease of vision, the gonioscopic finding of a grade 3 or 4 angle effectively rules out the possibility that these symptoms may have been caused by angle closure glaucoma.

Angle closure glaucoma presupposes an anatomically narrowed angle (0, slit, or 1) that can be rapidly closed off by iris dropping or being pushed against the trabeculum. Physiologic factors which determine the width of the anterior chamber angle are as follows:

(1) Place of iris attachment.
(2) Lens—increases in size with age.
(3) Thickness of iris—thicker in brown-eyed individuals.
(4) Development of ciliary muscle—thicker and more developed in hyperopes.
(5) Size of entire eye—smaller in hyperopes.
(6) Age—probably mainly changes in the size of the lens.
(7) Dilatation of the pupil—physiologic and with medication.
(8) Accommodation—reading.
(9) Heredity.
(10) Physiologic pupillary block.
(11) Congestion of uveal tract—emotional crisis, inflammation, unknown causes.

A completely similar pathologic process can cause angle closure by secondary changes in the lens, for example:

(1) Intumescent swelling with immature cataract.
(2) Rapid swelling after trauma with rupture of capsule.
(3) Subluxation forward, pressing the iris into the angle, or causing pupillary block.

Ophthalmologists are aware of the possibility that a mydriatic may produce an attack of acute angle closure glaucoma. Some have had the dramatic experience

of producing such attacks and have found that not all of them can be terminated by medical means alone. Since the pupils of many patients are dilated for refraction and ophthalmoscopy, it would be of great value to know in which patient the pupils could be dilated with impunity and in which the eyes might be precipitated into a state of acute glaucoma. In too many offices and clinics it is still routine to use tonometry as the guide to safety in dilating a pupil: in these offices it is felt that if tension is normal, it is safe to dilate. Actually, the level of the intraocular pressure is of no value in predicting which eyes may be precipitated into acute glaucoma. The factor which should be the guide is the width of the angle of the anterior chamber. If the angle is wide open, a grade 3 or 4, any mydriatic or cycloplegic drop can be used without fear. However, if the angle is narrow, grade 1, or a slit, one should be aware of the possibility of producing an acute rise of tension by mydriasis. If it is important to dilate that pupil this should be recognized as a calculated risk.

The extent of this risk was investigated by Sugar, who deliberately dilated the pupils of the normal eye in 20 patients with previous attacks of acute closed angle glaucoma in the first eye. He produced an acute rise of tension in six of these eyes, approximately one third. The tension in all six eyes was returned to normal with miotics. Not all of us, however, have been equally fortunate with our iatrogenic glaucoma.

If an eye has a borderline narrow angle, between grades 1 and 2, the chances are fairly good that the pupil can be dilated safely. However, in such a case it would be worthwhile to follow the patient carefully because the increase in lens size over the years may convert it into a 1 or even a slit. In order to give additional prognostic information it would also be worthwhile to gonioscope this eye with the pupil dilated and note the state of the angle at that time.

Although gonioscopy is the most accurate, it is not the only method of estimat-

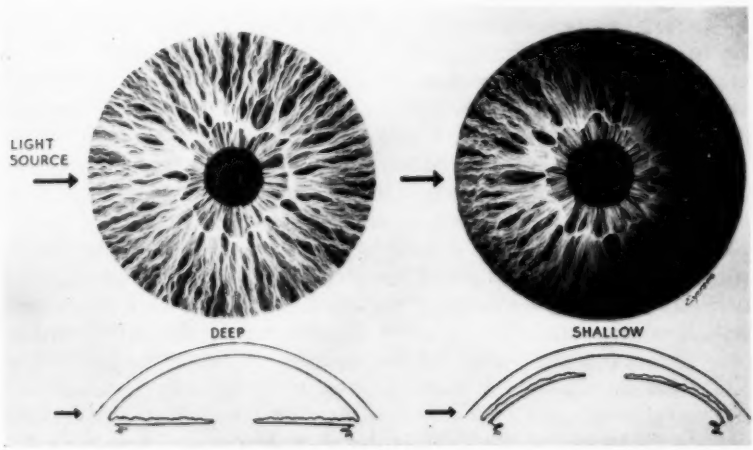

FIGURE 9. Method of demonstrating anterior chamber depth with a flashlight.

ing the width of the angle. The anterior chamber depth can be estimated by shining a flashlight beam across the iris plane from the side and noting the extent of the iris shadow (Fig. 9). However, the angle width is not always well correlated with the anterior chamber depth so this method is a rough one. More accurate is the use of the narrow slit lamp beam directed at an oblique angle at the corneoscleral limbus. This allows a good estimation of the distance between the cornea and iris at the limbus and correlates quite well with the gonioscopic findings. If still in doubt, gonioscopy should be performed before dilating this pupil.

When the term "angle closure" or "narrow angle" glaucoma is used, it is implied that the cause of the elevated intraocular pressure is the apposition of the iris to the trabecular region. For this mechanism to be at fault at least three fourths of the trabecular area, three quadrants or more, should be blocked by the iris apposition. The following case report illustrates this point:

A 50 year old woman complained chiefly of periodic headaches and recent blurred vision. The optic disks were normal. The visual fields showed early arcuate scotomas in each eye. The tension was R. 40 and L. 35 mm. Hg (Schiötz). Gonioscopy indicated the upper one-third of the angles closed in each eye and the two thirds grade 1. This patient had narrow angles, but the important thing to recognize was that the glaucoma level of her intraocular pressure at this time was not caused by the narrow angles. She had simple glaucoma, and her narrow angle was coincidental. The lower two thirds of her angle being open, even though narrow, should be adequate for the maintenance of normal pressure if the angle block mechanism alone were operative.

This diagnosis is of the utmost importance in the therapy of this patient. An iridectomy will not cure her glaucoma since pupillary block and angle closure are not the cause of her increased intraocular pressure. If any surgery is performed it should be some type of filtering procedure.

Could this patient be a candidate for a superimposed angle closure glaucoma? Yes, she very definitely could, with her anatomically narrowed angles. Her angle could be closed completely and develop a full-blown attack of acute angle closure glaucoma. If this occurred, and one had the benefit of knowing from previous gonioscopy that tension had also been elevated without the angle closure mechanism, one would know that an iridectomy would not cure the glaucoma even though it might relieve the acute attack and cure the closed angle component of the glaucoma. It would be necessary to use a filtering procedure along with the iridectomy to treat properly both causes of the glaucoma.

The typical attack of acute angle closure glaucoma is so well known that it will only be mentioned here. The essential point in making this diagnosis is that when the tension is elevated, gonioscopy would show the angle more or less completely closed. If corneal edema prevents the visualization of the angle through the contact lens, 1 or 2 drops of 50 per cent glycerine on the cornea will clear it for several minutes, long enough to see the angle gonioscopically.

In another case, a 45 year old man, who had had no previous eye complaints, developed discomfort in the right eye, with blurred vision and halos around lights. Examination revealed mild ciliary injection associated with a slightly

steamy cornea in the right eye. Vision was R. 20/40 and L. 20/20. Visual fields were normal. Tension was R. 70, L. 20 mm. Hg (Schiötz). The fundi were normal. The right pupil was slightly dilated and both pupils reacted to light. Gonioscopy revealed grade 3 angles bilaterally. This was apparently acute glaucoma, but it was not due to angle closure and, therefore, would not be benefited by an iridectomy. This patient had a glaucomatocyclitic crisis as described by Posner and Schlossman, and the glaucoma would subside spontaneously within a few days with or without medical therapy.

Following is still another example of the value of gonioscopy in differential diagnosis: A 60 year old woman had a sudden onset of right eye pain, blurred vision, nausea, and vomiting. Vision was R. 20/400 and L. 20/20. The right eye had a steamy cornea, ciliary injection, dilated pupil, and tension of 80 mm. Hg. Gonioscopy revealed the angle to be closed in the right eye and grade 3 in the left eye. This patient undoubtedly had an attack of closed angle glaucoma, but one should be suspicious of its cause. In almost all cases of primary narrow angle, the anatomic state of the narrow angle is bilateral. When one eye has a wide open angle and the other a narrow angle, there is usually some secondary factor operative in one of the eyes. This may be an immature cataractous lens with rapid intumescence narrowing the angle, or the lens may be subluxated forward causing a pupillary block with iris bombé and angle closure, or it may directly press the iris against the trabeculum. A malignant melanoma or ciliary body cysts may be present behind the iris, or even a retinal detachment with a cyclitic membrane may be forcing the iris lens diaphragm forward. It is important to consider these possibilities in a unilateral narrow angle because the basic cause must be recognized and treated.

Tonography has become a valuable diagnostic tool in glaucoma work. How does it correlate with the gonioscopic finding of narrow or closed angles? In angle closure glaucoma, between attacks and when the angle is open although narrow, tonometry and tonography are within normal limits and offer no clue to the potentiality of an acute attack of angle closure glaucoma. When the angle is closed, then tonography will of course show decreased coefficient of outflow. Immediately after an acute attack of angle closure glaucoma has been terminated, either spontaneously or medically, tonometry indicates a normal tension. Gonioscopy may show an angle that is so slitlike that the examiner cannot be certain whether there is sufficient access to Schlemm's canal or whether there are extensive peripheral anterior synechias blocking such access. Even with extensive peripheral anterior synechias the tension may remain normal, for a while at least, due to depression of aqueous inflow as a result of trauma to the ciliary body from the acute attack itself. In such a case, tonography can diagnose a decreased aqueous inflow and tell whether there still exists an obstruction to outflow. In still another situation of decreased coefficient of outflow with a narrowed but open angle, we also get diagnostic information, namely, that the narrow angle mechanism is not responsible for this decrease in the coefficient of outflow but rather that the patient has simple glaucoma in an anatomically narrow angle eye.

When gonioscopy reveals a very narrow angle that appears closed in several

places, one wants to know whether this closure is by simple apposition of the iris to the trabeculum or if there is an actual synechia present. This knowledge would have valuable therapeutic implications. The distinction cannot always be made, but several diagnostic procedures should be carried out. One is to shine a light into the opposite pupil while observing the eye in question with a gonioscope. The consensual pupillary contraction will frequently pull the angle open sufficiently to ascertain the point. Another aid is the use of a miotic followed by gonioscopy. If the extent of the peripheral anterior synechia still cannot be determined, it remains uncertain whether an iridectomy would suffice or whether a filtering procedure would be necessary because of hidden extensive peripheral anterior synechia which would prevent the iris from falling free. In such a case, if it has been decided that surgery is indicated, the method of gonioscopy on the operating table devised by Shaffer can be used (see Surgical Gonioscopy).

If there are no peripheral anterior synechias, the effect of iridectomy is seen beautifully by gonioscopy. Where prior to surgery the angle was closed or a slit, iridectomy breaks up the pupillary block and iris bombé mechanism and the angle landmarks open up, showing a grade 1 or 2 angle.

What are the effects of miotics or mydriatics on the gonioscopic picture of a narrow angle? Usually a miotic opens the angle a little by pulling the iris toward the pupillary margin and thinning it out. Occasionally, however, a miotic (especially one like Floropryl) will increase the pupillary block mechanism, causing a further "physiologic" iris bombé with additional narrowing or even gonioscopic closure of the angle. It is felt by some that this effect may be furthered in the case of Floropryl by congestion and edema of the iris and ciliary body, causing increased approximation of the iris to the trabeculum.

A mydriatic tends to pull the iris into the angle with thickening and bunching up of the peripheral iris, further narrowing or even closing the angle. However, this effect is sometimes counterbalanced by the reduction of the pupillary block mechanism in wide dilation of the pupil. In considering the effects of constriction and dilation of the pupil there are, therefore, two factors: (1) mechanical thickening or thinning of the iris in the angle, and (2) the pupillary block and iris bombé mechanism. Chandler feels that the net pressure raising effect of these two mechanisms is worse at mid-dilation than at full dilation. It is thought that in the mid-dilated position the pupillary block is still not broken and yet the iris is looser and, therefore, more readily pushed forward against the trabeculum.

At times one is faced with a patient who has had minor episodes of angle closure glaucoma with spontaneous reopening of the angle between attacks. It may be that surgery is not desirable at that time and it would be preferable to follow and treat this patient medically. Gonioscopic follow-up of this patient's angle offers an important guide as to safe continuation of medical therapy. Assuming that the eye has a narrow angle closed off by peripheral anterior synechias from 11 to 1 o'clock, and that three months later the angle is the same but that at six months the angle is closed from 9 to 3 o'clock, even though the tension is still normal with miotics: this gonioscopic extension of peripheral anterior synechias and angle closure indicates a progression of the process under

medical therapy and is a strong indication for surgery, i.e., an iridectomy. If there is further delay, there will be an extension of peripheral anterior synechias until three fourths of the angle is closed off, and then the slow rise of intraocular base pressure will occur which is typical of chronic angle closure glaucoma. A more radical operative procedure than a simple iridectomy will then be needed as at any time a complete angle closure may occur, resulting in an acute glaucoma.

If gonioscopy of an eye with previous inflammation or cataract surgery reveals an angle closed by extensive peripheral anterior synechias over three fourths of the circumference, the remaining one fourth being wide open, the eye will probably have an elevated tension and decreased coefficient of outflow; but this type of angle closure is to be differentiated from narrow angle glaucoma with corresponding apposition closure of three fourths of the angle. The important distinction is that in the former, a pupillary block, iris bombé mechanism is not operative and an iridectomy will not cure the glaucoma as it would probably do in the latter.

SIMPLE GLAUCOMA

The anterior chamber angle of an eye with simple glaucoma may be of any width, probably following the distribution of angle width in the general population. The block to outflow of aqueous is in the trabeculum, Schlemm's canal, or the aqueous veins. Since one cannot ordinarily see beyond the trabeculum, gonioscopy is not of real value in the diagnosis of this type of glaucoma. It is rare to see blood in Schlemm's canal in an eye with simple glaucoma. This is in contrast to normal eyes, of which about one third show blood in Schlemm's canal region during gonioscopy. The cause for this difference in behavior has not been determined, and discussion as to possible mechanisms is not pertinent to this paper. However, clinical observation during gonioscopy indicates that the presence of blood in Schlemm's canal in a patient in whom borderline glaucoma is suspected is additional evidence against the presence of glaucoma in this eye.

In simple glaucoma undisturbed by surgery or inflammation, peripheral anterior synechias are almost always absent. There may or may not be a number of iris processes which have to be distinguished from peripheral anterior synechias. The iris processes do not seem to be correlated with the presence or absence of glaucoma, except in juvenile glaucoma.

With time and progression of a glaucomatous process there is increased deposition of pigment in the trabeculum resulting in a more prominent trabecular pigment band. It is felt by some (François) that the presence or absence of pigment on Schwalbe's line and the trabeculum shows little if any correlation with the presence or absence of glaucoma. It is probable that the pigment does not materially decrease aqueous flow, unless possibly in such exaggerated conditions of pigment deposition as pigmentary glaucoma or glaucoma capsulare. There is normally a decreased translucency of the trabeculum with age, and some excellent observers, among them Barkan, think it is more marked in glaucoma. While most cases of simple glaucoma occur in open angles grading from 2 to 4, a small percentage may occur in anatomically narrow angles. In other words, the fact that a patient may have a narrow angle does not make him immune to simple

glaucoma. Since it is said that 5 to 10 per cent of the population over the age of 40 years have narrow angles, a corresponding number of patients with simple glaucoma should have narrow angles. They are consequently vulnerable to an attack of acute angle closure glaucoma. If this acute glaucoma is cured by iridectomy there will still remain the underlying simple glaucoma which will require treatment.

CONGENITAL GLAUCOMA

The term "congenital glaucoma" applies to those cases of increased intraocular pressure in which the decreased aqueous outflow is due to defective embryologic development of the eye. It is known that faulty genes may cause developmental defects first to appear some time after birth. In infantile glaucoma the symptoms are present at birth or appear within the first three years of life, resulting in the distended eyeball known in the past by the picturesque terms "buphthalmos" or "hydrophthalmia." Cases occurring in the 3 to 35 year age group are known as juvenile glaucoma and are not an etiologically pure group. Included may be late developing infantile glaucoma as well as early developing angle closure glaucoma or chronic simple glaucoma.

INFANTILE GLAUCOMA

In infantile glaucoma the iris does not insert on the anterior ciliary body. The underdeveloped anterior iris inserts directly into the trabeculum, forming, in effect, a "synechia" which covers one tenth to one half of the angle wall. As the gray strands and radial blood vessels reach the inner surface of the trabecular wall, they seem to be slightly picked up on the translucent tissue representing the uveal portion of the trabeculum. In a high tension eye the blood vessels may be so engorged as to resemble a hemangioma. Through the thin anterior iris stroma the pigment layer forms arcade-like sectors.

In early infantile glaucoma, when the tension has been normalized, it is usually possible to see blood in Schlemm's canal by the use of jugular compression as shown by Scheie. After long continued pressure the canal is evidently compressed and no longer patent. This is the reason early surgery is so important.

In performing a goniotomy the diagnostic examination is performed with the usual equipment. Particular attention is paid to the height of the iris insertion, the position of blood vessels and of Schwalbe's line. If visibility is poor because of corneal edema, all the epithelium should be scraped off the cornea. In essence a superficial trabeculotomy is performed just below Schwalbe's line. This gives access of aqueous to Schlemm's canal. The technique used is described by Barkan.

JUVENILE GLAUCOMA

As stated before, some of these cases resemble infantile glaucoma gonioscopically. Some look like ordinary open angle chronic simple glaucoma. There is a group of cases which seem to have more evidence of imperfect angle development than normal. The trabeculum may be longer than usual and the line of Schwalbe quite prominent. Iris processes, small and large, or entire sheets of iris stroma

may circle the angle recess, extending in a variable pattern and for varying distances over the trabeculum. Variations of this pattern are seen in 15 per cent of normal controls according to Burian, Braley, and Allen. The more severe forms of this angle anomaly make up the syndrome of Axenfeld, or posterior embryotoxon, which is inherited in a dominant pattern according to Falls. Increased tension may never become a problem in these cases, or it may appear as late as the fifth decade.

Pigmentary glaucoma, described by Sugar and Calhoun, must be included in the juvenile group. It is diagnosed gonioscopically by the tremendously prominent brown-black trabecular pigment band, frequently iridodonesis, and by a Krukenberg spindle of pigment on the posterior cornea.

GLAUCOMA ASSOCIATED WITH OTHER CONGENITAL ANOMALIES

Aniridia, or irideremia, is inherited as a dominant genotype. The rim of remaining iris is usually visible by gonioscopy. The stump of iris may be against the trabecular area, sometimes nearly to Schwalbe's line.

Nevus flammeus, or the Sturge-Weber syndrome, is a congenital condition which is usually unilateral. The angle looks somewhat like that in infantile glaucoma, though some cases have greater vascularity of the iris and angle. There is often an associated angioma of the choroid and of the brain. It is inherited recessively.

Neurofibromatosis presents changes involving the face and eye. Anderson states that hypertrophied ciliary nerves and a diffuse thickening of the choroid appear to be constant changes. The characteristic angle change is the presence of iris-like tissue wrapping around the angle wall.

In these three conditions there is a block to outflow through tissue blocking the trabeculum. Since there is the possibility of improving the condition by goniotomy, this procedure should be used before trying the mutilating types of surgery.

SECONDARY GLAUCOMA

The cause of glaucoma should be determined, if at all possible in all cases. Gonioscopy may be the etiologic key. This is particularly true in conditions which result from iris contact to the trabeculum, blocking aqueous outflow. The following is modified from Sugar's classification of secondary glaucoma.

I. The Narrow Angle Group

Since its etiology is well known, one might include "angle closure" or "acute" glaucoma as the prototype of such cases. All tend to have shallow chambers, narrow or occluded angles, and usually some degree of pupillary block interfering with the free flow of aqueous into the anterior chamber.

(*a*) *Seclusion of Pupil Causing Iris Bombé.* An early iris bombé is sometimes seen best by gonioscopy. This is especially true if the iris is firmly fixed to the lens by posterior synechias over a large part of its surface. Then the iris bulge is only seen peripherally and may be missed without gonioscopy.

(*b*) *Lenticular Intumescence.* Progressive shallowing of the anterior chamber results eventually in a typical angle closure glaucoma. The angle seen by gonioscopy is closed over most or all of its extent during the period when the intraocular pressure is raised. The role of the lens is suggested by finding an immature cataract with numerous water clefts or lamellar separation. This is especially true if the opposite eye does not have these lenticular changes and shows a normally deep anterior chamber and wide open angle. Therapeutically this is an ideal situation, insofar as the closed angle glaucoma and the cataract may both be cured in one operation by simply removing the lens.

(*c*) *Epithelial Ingrowth into the Anterior Chamber.* Uusually the epithelium coats the trabeculum and an open angle type of glaucoma occurs. Occasionally, however, if this condition results in epithelial cells blocking the free flow of aqueous through the pupil, the chamber will then become shallow and a secondary angle closure glaucoma will ensue.

(*d*) *Aphakia with Pupillary Block.* When the pupillary margins of the iris and the edges of any existing iridectomy are sealed by synechias to the anterior vitreous face or to lens or lens capsule remnants, a condition similar to iris bombé results. If the vitreous face is strong enough a shallow chamber occurs. In an aphakic eye if the angle is not wide open, that is, if the angle is grade 1 or 2, and if the intraocular pressure is elevated, a pupillary block mechanism for the glaucoma should be suspected. The vitreous is so closely opposed to the iris, with or without synechia to it, that the normal flow of aqueous from the posterior to the anterior chamber cannot take place. In these cases the iridectomy opening undoubtedly is not functioning. In such an eye with extensive posterior synechias, if the anterior hyaloid face of the vitreous ruptures, vitreous will be pushed into the anterior chamber by the aqueous collecting behind the iris. The mechanism is the same, but in the first case there is a shallow chamber, and in the second a deep chamber full of vitreous, both with increased tension. These eyes occasionally respond well to mydriatics, but frequently an additional iridectomy is needed to cure the glaucoma.

(*e*) *Partial Dislocated Lens.* Occasionally a pupillary block mechanism develops with a syndrome similar to that of aphakia with pupillary block. Iridodonesis, which may or may not be seen grossly or with the slit lamp, is almost always seen gonioscopically. Often the anterior chamber angle is much narrower in one part of the angle than in another, due to tilting of the lens. Another characteristic of this type of glaucoma is that the gonioscopic picture may vary a great deal from one examination to another. For example, an examination on a day when the pupillary block mechanism is operating will show the angle markedly narrowed or even closed, perhaps without iridodonesis; while on a subsequent day the angle may be of grade 2 or even grade 3 width and may show definite iridodonesis.

(*f*) *Miscellaneous Conditions.* Lens dislocated into the anterior chamber, spherophakia, retrolental fibroplasia, and massive hemorrhage into the posterior ocular segment are included in this group.

II. The Peripheral Anterior Synechia Group

(*a*) *Following Angle Closure.* After the pupillary block mechanism present in group I cases has been relieved, the peripheral anterior synechias which had formed will remain. These prevent outflow of aqueous at the point of the synechias, and a chronic form of glaucoma may continue. Synechias, which are always pathologic, can be recognized and differentiated from the physiologic iris processes as discussed previously in this paper. Cyclodialysis or a filtering procedure is usually the indicated therapy if miotics fail.

(*b*) *Aphakia.* The average aphakic patient shows a wide open grade 4 angle except in the region of the iridectomy. Here, there is commonly a peripheral anterior synechia at either margin of the iridectomy; the remaining peripheral flap of iris may occlude the angle wall and occasionally be adherent to the corneoscleral incision. If some complication of cataract surgery ensued, e.g., vitreous loss, iris prolapse, iridocyclitis, or postoperative flat anterior chamber, the peripheral anterior synechias may be more extensive. If the synechias are sufficient to occlude more than three quarters of the angle circumference, glaucoma will probably be present.

(*c*) *Glaucoma Following Collapse of Anterior Chamber with Perforation of the Globe.* The longer an anterior chamber is collapsed, the more extensive will be the peripheral anterior synechias, and the more severe will be the resulting glaucoma.

(*d*) *Essential Progressive Atrophy of the Iris.* Glaucoma is a late complication which is most difficult to treat successfully. Gonioscopy reveals the remnants of iris to be flapped up against the angle of the anterior chamber, occluding it by peripheral anterior synechias. These synechias are present on the side toward which the pupil is drawn, and also on the side of the iris holes. When these synechias cover three quarters of the angle circumference, glaucoma is generally present.

(*e*) *Iridocyclitis.* Areas of edema or granuloma formation at the iris root result in moundlike peripheral anterior synechias. These may coalesce to form more extensive areas which then resemble those seen following the pupillary block or anterior chamber collapse glaucomas. Keratic precipitates can sometimes be seen on Schwalbe's line and on the trabeculum by gonioscopy when they are invisible by simple slit lamp examination. These are occasionally large enough to touch the iris. Their organization then produces a localized synechia.

An important corollary to the diagnosis of peripheral anterior synechia glaucoma *without a pupillary block component* is that pupillary dilatation does not cause a significant narrowing of the anterior chamber angle. Therefore, even though these eyes may be glaucomatous and even though a large part of the angle circumference is occluded by peripheral anterior synechia, mydriatics may be used for examination of the fundus without danger of precipitating an attack of acute angle closure glaucoma.

III. Open Angle Secondary Glaucomas

In many instances of open angle glaucoma, gonioscopy is of no help in determining the etiology. This is because the mechanism at fault is farther beyond the

inner trabeculum than one can see gonioscopically. Some clues may be gained, however, and occasionally these are diagnostic.

(*a*) *Intense Pigmentation of the Trabecular Pigment Band.*

(1) Pigmentary glaucoma:—This condition generally becomes manifest in young men, myopes, with Kruckenberg spindles on the corneal endothelium, and slight iridodonesis. Large hands and feet may be present as part of the syndrome. It is one form of so-called juvenile glaucoma. The iridodonesis, as stated elsewhere, is sometimes visible only with the aid of the gonioscope.

(2) Glaucoma capsulare:—Some patients with simple glaucoma show flecks of white dandruff-like material on the surface of the lens, the pupillary margin, the zonule fibers, and in the angle of the anterior chamber. These flecks may be visible only by gonioscopy in some instances. It was originally thought that all of this material was exfoliated from the lens capsule, but it is now felt that it arises from other structures within the eye as well as the lens capsule. Unfortunately the glaucoma is usually not cured by removing the lens which was the supposed source of the material.

(3) Old glaucoma, iritis, or other intraocular disease may cause some increase in pigmentation of the trabecular pigment band.

(4) Megalocornea often has intense pigmentation of the trabecular pigment band.

(*b*) *Rubeosis iridis.* Neovascularization of the trabeculum is often the first sign of onset of rubeosis. As neovascularization progresses, extensive peripheral anterior synechias result. The causes of the condition are diabetes, occlusion of the central retinal vein, and, occasionally, repeated vitreous hemorrhages.

(*c*) *Iridocyclitis.* It is not uncommon in eyes with iridocyclitis that a secondary glaucoma ensues. In some of these eyes, peripheral anterior synechias have not formed and the anterior chamber angle is open gonioscopically. In these cases the glaucoma is probably due to edema, exudates, and cellular debris clogging the outflow channels beyond the range of gonioscopic visibility.

(*d*) *Contusion of the Globe.* If the angle is open gonioscopically, the mechanism of the glaucoma here is probably similar to that in iridocyclitis.

(*e*) *Phakolytic Glaucoma.* Eyes containing mature or hypermature cataracts may develop glaucoma characterized by large particles floating in the anterior chamber as seen by slit lamp examination. Gonioscopy shows open angles. The mechanism of the glaucoma is felt to be obstruction of the outflow channels by the large macrophage engulfed lens particles and the inflammatory edema resulting from liberation of the toxic lens products. Cataract extraction cures the glaucoma.

(*f*) *Blood in Schlemm's Canal.* Although this is usually a sign against the presence of glaucoma, it may be a clue to glaucoma from increased venous pressure caused by orbital pressure from tumor or inflammation, or from an arteriovenous fistula.

(*g*) *Endothelial Proliferation.* The development of hyaline membranes in the angle is found in chronically inflamed eyes.

(*h*) *Tumor Growth in the Angle.* Gonioscopy may be the only means of clinically

diagnosing an annular melanoma of the ciliary body causing a secondary glaucoma.

(*i*) *Epithelial Downgrowth.* A translucent membrane is seen on the angle wall and iris with flattening of the iris markings.

SURGICAL GONIOSCOPY

I. Preoperative Examination

Preoperative gonioscopy is of great importance in determining the etiology of the glaucoma so that appropriate surgery can be chosen. It is also useful in noting the presence of large blood vessels or areas of iris atrophy to be avoided. In doing goniotomy or goniopuncture it should be used in deciding the area of angle to be operated and in noting landmarks under greater magnification than is usual in angle surgery.

II. Surgery Under Gonioscopic Control

(*a*) *Goniotomy and Goniopuncture.* The principal use of surgery under gonioscopic control is in goniotomy as described by Barkan. Without such visualization the surgeon loses the visual control which adds so much to the precision and safety of the procedure. Its use adds to the precise placing of a goniopuncture incision.

(*b*) *Cyclogoniotomy.* This is a method of producing a cyclodialysis by shearing the ciliary body from its attachment at the spur by means of a goniotomy knife under gonioscopic control. It has recently been described by Barkan.

(*c*) *Closure of Cyclodialysis Clefts by Diathermy.* In hypotony following cyclodialysis, it may be necessary to close the cleft. This has been possible without gonioscopic control, but would be better controlled by its use. It is possible to look through a surgical contact lens as the sclera is indented over the cleft with an electrode. In a soft eye the sclera can be seen to push down against peripheral iris in the area of the cleft. The high frequency current is then applied at this position.

(*d*) *Choice of Surgery in Angle Closure Glaucoma.* One of the big problems in narrow angle glaucoma and in pupillary block secondary glaucoma is the estimation of the extent and permanence of anterior synechia formation. It has been the custom to do an iridectomy early in a first attack of acute glaucoma, and an iridencleisis after 36 hours or with a history of several attacks. Such an empiric rule may often be right, but it is just as likely to result in a mutilating fistulizing operation when the more physiologic iridectomy might be completely effective.

It is suggested that iridectomy be performed first and the anterior chamber be reformed after single tying the McLean suture. Then a sterile contact lens is placed on the eye and gonioscopy performed. If the iris has dropped free from the trabeculum, further surgery is unnecessary. If synechias are still present, they may be freed by a synechialysis, using a spatula passed into the anterior chamber. If this is ineffective, as judged by a second gonioscopic examination on the operating table, a cyclodialysis can be done in the area of the synechias through a second incision or through the original incision. If one is enthusiastic

about iridencleisis, a peripheral iridectomy may be converted into an iridencleisis. In any case a logical decision may be made based upon visually proved presence or absence of peripheral anterior synechias at the time of surgery.

POSTSURGICAL GONIOSCOPY

After almost any intraocular operation, scarring and synechia formation can be seen gonioscopically. Following cataract surgery there are frequently small synechias at each edge of an iridectomy and often at the ends of the incision. If the anterior chamber has been collapsed following surgery, the synechias are usually much more extensive. If they block a large enough area of the trabeculum a rise of tension will result. It is impossible to say what degree of angle block will result in glaucoma as it will depend on the facility of outflow. With healthy outflow channels, two thirds of the circumference can be closed by peripheral anterior synechia before a rise in base pressure can be expected.

There is a characteristic appearance to the angle after glaucoma operations which in some cases is of prognostic significance:

(*a*) *Iridectomy.* In angle closure glaucoma without permanent peripheral anterior synechias the angle will open from a 0 to a 1 or a 2 angle after iridectomy. This widening occurs over the whole angle circumference and not merely in the area of the iridectomy. In such an instance a cure can be expected. Pupils can be safely dilated in such cases and gonioscopy shows the angle open during mydriasis.

(*b*) *Iridencleisis.* The incarcerated iris should wedge apart the inner corneal incision, forming a small cleft in successful cases. However, some such cases may be closed by scarring in the episcleral area. Others, without obvious clefts, seem to be effective through channels which are gonioscopically invisible.

(*c*) *Trephine and Sclerectomy.* The round or oval inner incision site is usually easily seen. Iris, lens capsule, vitreous or ciliary processes may be incarcerated in the opening. This is particularly true if the incision is in the posterior trabeculum. The filtration may also be blocked in the intrascleral or episcleral area beyond the range of gonioscopic vision.

(*d*) *Cyclodialysis.* In a successful cyclodialysis there can always be seen a cleft into the suprachoroidal space. If no such cleft is present it is quite probable that the tension will again become elevated in the course of the next few weeks or months. Late closure of the cleft occurs. In such cases gray connective tissue can be seen at the edges of the cleft. These continue to grow and reattach the ciliary body to the sclera. This may be at a point behind the original attachment at the spur, resulting in a gonioscopically apparent cleft without communication into the suprachoroidal space.

(*e*) *Goniotomy.* In infantile glaucoma in which the line of iris attachment is high on the trabeculum, there is marked recession of the attachment in the area of the goniotomy. The angle wall looks cleaned of translucent trabecular material in the zone of the incision. True secondary synechias can also form onto the incision line.

(*f*) *Goniopuncture.* In successful goniopunctures a tiny gaping oval opening can be seen in the trabeculum.

MISCELLANEOUS

Tumors. Particularly in iris tumors, gonioscopy is of great importance in determining the peripheral limits of the lesion. If free of the anterior ciliary body excision by iridectomy is feasible. Some tumors, particularly melanomas and cysts of the anterior ciliary body, may only be seen gonioscopically through the widely dilated pupil either in the angle or on the ciliary body or posterior iris.

Foreign Bodies. After perforating injuries of the eye, foreign material may drop down into the angle and be hidden from view. Many cases of chronic iritis have been cured by the gonioscopic observation of a foreign body in the angle and its subsequent surgical removal.

Iridodialysis. Following contusion of the globe an iridodialysis may be produced which may only be visible gonioscopically. Knowledge of this damaged area may be important if diathermy is needed to stop recurrent hemorrhages.

Clinical Practice

ACCOMMODATION AND REFRACTION

THE MANAGEMENT OF ANISOMETROPIA

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Eye, Ear, Nose & Throat Month., 1957, *36:* 217–222

Anisometropia of a significant degree is found in about 10 per cent of refractions. The forms encountered include varying inequalities of hyperopia, myopia, or astigmatism in all possible combinations, not excepting antimetropia where one eye is hyperopic and the other myopic. Anisometropia may be congenital, or it may be the result of developmental changes in youth or age, or again it may have been acquired from conditions changing the refraction of the cornea or lens, the length of the globe, or the position of the macula. Anisometropia may be accompanied by binocular vision, simultaneous vision without fusion, monocular vision, or alternating vision, one eye being used for distance and the other for near. A disorder often associated with anisometropia is muscular imbalance.

In hyperopic anisometropia, one eye may be more or less amblyopic. Since the accommodation is normally equal, the child without glasses can accommodate for a clear image in only one eye. The other eye receives a blurred image both for distance and near and accommodative amblyopia tends to result. Children adapt themselves readily to any type of anisometropic correction. If one eye is amblyopic, its vision is generally improved by temporary occlusion of the better eye.

The principal cause of discomfort in anisometropia is the artificial heterophoria created whenever the eyes move from the primary position, especially the induced hyperphoria when looking down. The other disturbing factors are less important. No form of optical compensation for anisometropia should be prescribed without first considering the influence of any intrinsic hyperphoria that may be present for distance or near. Hyperphoria is usually incomitant, that is, it is greater in the primary position than at the reading level of the eyes, or vice versa. The tests for hyperphoria should be made in the following manner: (1) The dominant eye should be determined with the corrective lenses; (2) the tests should then be made with the corrective lenses removed; (3) the examination can be made more easily in a dark room, and a large spotlight, 2.5 cm. in diameter, is advisable for distance fixation; (4) the red glass should be placed over the dominant eye,

and a white ribbed Maddox rod over the other—the measuring lenses are placed over the Maddox rod; and (5) the examination for hyperphoria for distance should be made with the eyes in the primary position, and that for near with the patient holding a small fixation light in the habitual reading position with the eyes turned down about 20 degrees.

The simplest and least equivocal of the many methods of determining ocular dominance is the sighting test. A hole the size of a quarter is made in the center of a sheet of cardboard or darkened x-ray film the size of standard typewriter paper. The patient, holding the sheet at arm's length with both hands, gazes at the distant fixation light, gradually bringing the sheet towards the face. If the gaze is maintained while the sheet is being moved, the hole will overlie the dominant eye at the end of the movement.

Hyperphoria is not affected by accommodation and errors in its determination will be avoided if corrective lenses are not used. Lenses complicated the picture because of the differential prismatic effect of an anisometropic correction. Moreover, the trial lenses themselves can introduce adventitious prismatic effects. Schilling found decentration errors of 0.5Δ to 3Δ in 43 per cent of non-precision lenses and in 13 per cent of so-called precision lenses.

The natural fixation can be altered by the Maddox rod or the applied prism. In the absence of a test prism one fixes usually with the eye looking through the red glass rather than with the eye behind the Maddox rod; but the obscuration produced by the addition of a prism can shift the fixation to the opposite eye. To assure continued fixation of the eye behind the red glass, the measuring prisms must be placed over the Maddox rod. In hyperphoria for distance only, the prismatic correction should be prescribed when it is helpful in neutralizing the induced anisophoria of anisometropic lenses, which often happens, but not otherwise.

Comparison of the data obtained with the dominant eye maintaining fixation with those obtained after a change of fixation indicates the muscle that is involved and so supplies information that may be of clinical interest. Occasionally the intrinsic vertical muscle balance is normal and the prismatic differential at the reading level must be optically compensated.

In some patients with high anisometropic myopia, when the corrected acuity of each eye is good, it is often wise to abandon any attempt to secure binocular vision with its attendant difficulties, and to promote instead alternating vision, adapting one eye for distance and the other for near vision. With the use of one eye at a time the demand for balanced muscular activity is eliminated and symptoms due to incoordination cannot arise. Because of the unequal progression of myopia, many such patients have developed a natural tendency to this alternating vision. In children and young adults, however, every effort should be made to maintain binocular vision because an undercorrected eye may turn out. Likewise, when binocular vision is well established, the substitution of alternating vision should not be attempted. If tried, it will not be tolerated. When clearly indicated, arrangement for alternating vision improves the appearance of the glasses and also eliminates the need for bifocals. When useful vision

is present in one eye only, the patient should be relieved of an unsightly anisometropic correction from which no benefit is derived, whether squint is or is not present. Even if the corrected vision of the amblyopic eye is 20/200, the prescription of balanced lenses is to be preferred.

Contact lenses are an excellent, and sometimes the only, solution for anisometropia, as in monocular aphakia and monocular high myopia. Supplementary spectacles usually add to the visual efficiency of the correction.

Comment: This excellent paper by a well known authority in refraction and ocular motor problems contains much that is of value and directly applicable in the average ophthalmologic practice.

In tests for heterophoria, the author points out the desirability of the use of a red glass over the dominant eye and a white multiple Maddox rod in front of the other. Dissociation methods, to be effective in permitting the measurement of heterophoria, must provide a type of dissociation in which there is no possibility of the patient fusing the two objects. In lateral heterophoria, the test must also be designed so as to preclude the possibility of accommodative convergence interfering with the measurement of the basic imbalance. As Lebensohn points out, inasmuch as accommodation is not involved in the measurement of vertical imbalance, the Maddox rod and red glass combination is most suitable in these conditions. In lateral heterophoria, however, the use of the Maddox rod and red glass very often results in a faulty determination due to the lack of precise control of the accommodation for any given fixation. This is especially true with lateral heterophoria determinations at the near point. Because the presence of esophoria or exophoria at the near point is primarily dependent upon the amount of accommodative convergence at that point, changes in accommodation, such as might be due to the relatively poor definition of the dissimilar images produced by the Maddox rod and red glass, would result in inaccurate and probably unstable near point heterophoria readings.

For an accurate determination of near point exophoria or esophoria, therefore, adequate control of accommodation is necessary. This can be obtained by the use of a dissociating vertical prism with fixation upon a single letter small enough to require precise accommodation by whichever of the two eyes has it imaged upon its macula.

Prism dissociation for vertical heterophoria determinations, however, is not very practical because of the considerable fusional amplitude in the lateral direction possessed by the average person. To obtain the lateral dissociation required for vertical heterophoria tests, a considerable amount of prism power would be necessary, with a consequent large separation of the dissociated images and a consequent difficulty in judging when the one is higher than the other.

Practically all available information indicates that probably a majority of individuals with apparent intrinsic hyperphoria are really incomitant, and thus actually hypertropic. Fortunately, however, the incomitancy in many of these individuals is not marked, and with a suitable prism correction base up or down, fusion may be secured, persisting through the normal range of vertical fixation.

Induced hyperphoria as the result of anisometropic lens corrections, however, offers a different and even more formidable problem. Prepresbyopic individuals who do not have bifocals often solve the problem by moving the head more and the eyes less, and thus keeping the visual line more through the optical center of the lenses. In bifocal corrections, of course, this is not possible, and if comfortable single binocular vision is to be attained, the patient must either wear a separate pair of glasses for near with the optical centers lowered, or have some form of optical compensation in the bifocal segments for the induced

heterophoria. If the latter is not too much in amount, a compensation for the induced heterophoria may be obtained by using different types of bifocal segments with varying diameters but with the same height, such as using a wide Ultex segment in one eye and a small horseshoe fused segment in the other. When wearing bifocals, a patient usually will look through the base lens about 8 mm. below the optical center, and the prismatic effect of the base range at that point can be found by the use of the Prentice formula:

$$\Delta = D \times d$$

Where Δ = prism diopters
D = lens diopters in base lens or segment
d = distance in mm. from optical center of either base lens or segment

In calculating the combined prism power of the base lens and the segment at a given distance below the optical center, the prism power at that point of the base lens must first be calculated, then the prismatic power of the segment at the same point, and the two added algebraically to obtain the combined effect. When this process has been carried through in both the right and left eye lens combinations, the difference between them will indicate the induced heterophoria. For instance, if a convex right lens is found to have 3Δ base up at a point 8 mm. below the optical center and the prismatic effect of a stronger convex left lens at the same distance is 6Δ base up, the combined effect would be equivalent to 3Δ of right hyperphoria. Judicious use of an Ultex bifocal in the left eye and a smaller fused bifocal in the right would reduce, depending upon the power of the segment add, the induced hyperphoria to a level which might be capable of compensation by the vertical fusional vergence reflexes. To carry out such calculations, it would be necessary to know the position of the upper margin of the bifocal in relation to the optical center of the base lens in order to calculate the prism power derived from the decentration of the segment itself.

This type of calculation can also be used as a basis for the prescription of prism segments. These, however, are somewhat difficult to obtain and are limited in their effect, so that they are not often prescribed in the cases under consideration.

Much experience has demonstrated that few opticians are capable of understanding and performing the calculations prescribed above and that, although the procedures are simple, specific directions on the prescription for lenses are usually necessary. In selected cases these procedures often pay off in greatly increased comfort and visual efficiency.

Contact lenses in anisometropia, especially that due to monocular aphakia, must usually be supplemented by conventional glasses with a bifocal on the aphakic eye, even if the unoperated eye has sufficient accommodative power. If the unilateral bifocal is focused for the point at which the individual commonly holds his near work, the combination often is very satisfactory. In other cases, there is residual discomfort even with such a combination, and this may be due to aniseikonia which in turn may be eliminated or lessened by the use of a contact lens which creates a myopic condition which is then neutralized by concave lenses in spectacles, as suggested by the author.

EDWIN F. TAIT

THE CONJUNCTIVA AND CORNEA

IS EPIDEMIC KERATOCONJUNCTIVITIS A VIRUS INFECTION?

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Deutsche med. Wchnschr., 1957, *82:* 100; German Med. Month., 1957, *2:* 101–103

Infections with the adenovirus, or APC (adenoido-pharyngeal-conjunctival) virus, of which 14 different types have already been described, are becoming of increasing clinical importance.

In Germany there have been reports of an epidemic in Hamburg which affected hundreds of persons, mainly school children. The epidemic was characterized by fever, rhinitis, pharyngitis, papillitis of the tongue, cervical lymphadenitis, and especially conjunctivitis. The diagnosis of an adenovirus infection was based upon a positive neutralization and complement fixation test in four pairs of serums.

Our investigations were concerned with a syndrome which has been known in Germany for a long time and has been described under the name of keratoconjunctivitis. This acute conjunctivitis followed by a keratitis, which is variously described as keratitis nummularis, keratitis maculosa, keratitis subepithelialis centralis, or superficial punctate keratitis, has a very benign course, with some lassitude and, rarely, a subnormal temperature. It was suspected from the beginning that a virus was the causative organism. Although a number of viruses have been isolated and described, it has as yet not been possible to prove their etiological significance.

In South Baden there have been outbreaks of epidemic keratoconjunctivitis every year during the summer months of the last five or six years. The disease is only infective before the first symptoms appear and any attempts at isolation of the infection are, therefore, usually not effective. A few isolated attacks of the disease among patients of the eye clinic and an epidemic in a neighboring sanatorium affecting over 50 persons within three weeks gave us the opportunity for the following study.

Twenty-six patients were specially examined and had typical signs and symptoms. All of them had a sensation of a foreign body in the eye, a feeling of pressure and irritation. An acute conjunctivitis developed and was often misdiagnosed as being due to a foreign body. In the epidemic in the sanatorium the initial signs were slight redness and swelling of the caruncle and of the plica semilunaris with slight edema of the eyelids. Within 24 hours there was a generalized hyperemia of the tarsal and bulbar conjunctivae followed by follicular hypertrophy of the corneoconjunctival junction resembling frog's spawn. In most of the cases larger petechiae in the conjunctiva were observed; in three patients a dirty pseudomembrane developed.

At the start of the disease the preauricular lymph nodes on the side of the infection invariably enlarged to the size of a hazelnut. In one case the submandibular lymph glands persisted for three months after the eye infection had subsided. The most striking finding was the relatively small secretion of the highly inflamed conjunctiva. Examination of the secretion revealed monocytes and leukocytes, but no bacteria.

Eight to 14 days after the start of the disease the acute conjunctivitis began to subside, but the irritation increased and a superficial punctate keratitis developed. A few days later typical subepithelial nummular infiltrations of the cornea could be observed. The central infiltration could be stained with fluorescein and healed with scar formation within two to three weeks. In only 2 of the 26 patients the disease subsided while still in the state of superficial punctate epithelial lesions; there was no scarring. If one eye became infected after the other (usually within the period of 11 days), the scarring mainly occurred in the eye which was affected first; this seems to show that there was some production of antibodies. In the rare cases where both eyes became simultaneously infected both developed scarring to a similar degree.

All attempts to transmit the causative organism to animals, either from conjunctival washings or by swabbing the cornea, were unsuccessful. Infant and adult mice, guinea pigs and rabbits were inoculated in various ways (corneal, intracerebral, intramuscular, and intraperitoneal).

In October 1956 we had an opportunity to test the collected serum samples by complement fixation with type RI 67 (APC 4). In seven cases only single serums were obtainable; five of them gave a positive reading. These serums were obtained during the acute phase of the disease. In those cases where several serums were obtained antibodies were demonstrated in every patient. Twenty-three showed an increase of antibodies. We deduce from these observations that it is probable that the epidemic is caused by an adenovirus.

There have already been reports of the isolation of adenovirus in epidemic keratoconjunctivitis. Jawetz was able to isolate type 8. The adenovirus group has a common complement fixation antigen. Differentiation into types is possible only after neutralization. The complement fixation test is, therefore, especially useful in the diagnosis of all types of this infection. On the other hand, it does not differentiate between the various types of the virus.

Studies into the frequency of these infections, which are about to be published, have shown that a high percentage of the population is affected. In examining 170 persons of different ages we found that 98 per cent of children under six months of age showed antibodies, but in children six months to two years of age the percentage had risen to 50 per cent. It then remained steady around 40 per cent and dropped to 25 per cent after the age of 25. Because of this high percentage of antibodies in the population, only a marked increase in antibodies has any pathologic significance.

Comment: In 1952 Bieling reviewed what was then known about epidemic keratoconjunctivitis, a disease well known to ophthalmologists and encountered frequently in Eastern and Western Germany since 1954. Several investigators many years ago had

reported the successful isolation of a virus without, however, being able to demonstrate this virus to be the causative agent of epidemic keratoconjunctivitis. In 1943 Sanders reported the isolation of a virus after many passages through tissue cultures. It was shown later to be identical with the St. Louis encephalitis virus. Patients who had typical epidemic keratoconjunctivitis did not have neutralizing antibodies to the Sanders virus later, a hint that the cases observed in recent years were not caused by this agent. Whether the original Sanders virus has been lost in mouse passages cannot be established now. Also, reports on isolation of herpes virus, primary mouse pathogenic agents, and viruses grown on chorioallantoic membrane, declaring them to be the causative agents, could not be confirmed.

In 1955 Jawetz reported on a new APC virus isolated from conjunctival washings from a 50-year-old sailor who had just arrived in San Francisco from Asia. The patient demonstrated the classical picture of the disease with acute pseudomembranous bulbar and tarsal conjunctivitis and preauricular adenopathy, followed by a keratitis which led to the characteristic round infiltrations in the cornea and healed by scarring. There were no elevated temperatures or other signs of an upper respiratory infection. The half-sister of the patient fell ill with the same signs and symptoms 10 days later. HeLa cell cultures showed, on the seventeenth day after inoculation, cytopathogenic effects resembling to a high degree those of the APC viruses. The virus also had the complement fixing antigen of this group. It could not be neutralized by the antibodies of the types then known. It was therefore named type 8 of the APC viruses. During the acute and convalescent stages of the disease the patient had an increase in neutralizing antibodies against this type.

Meanwhile more type 8 strains were isolated from typical cases in the United States and in Scotland. Volunteers infected with type 8 developed an epidemic keratoconjunctivitis. Studies employing the type-specific neutralizing antibodies as a diagnostic aid were made in the United States, Canada, Switzerland, Italy, and Japan. Ninety-five per cent of 70 patients showed positive results, whereas only 7 per cent of the 140 control patients in the same areas had antibodies against type 8. Recent studies in Germany point in the same direction. Rhode and Wolfersdorf have reported an epidemic in Glauchau, Saxony. They obtained virus growth on the cornea of chick embryo. These viruses are not yet identified, but they may be adenoviruses, since animal inoculations gave no results. We studied a hospital outbreak; of 25 patients examined 23 showed a rise in complement fixing antibodies against adenoviruses during the acute and convalescent stages of the disease. From conjunctival washings a cytopathogenic virus could be grown on monkey kidney cells, but it has not yet been identified.

Laboratory findings to date strongly point to the assumption that type 8 is the causative agent of the cases of epidemic keratoconjunctivitis now being observed, although in several instances of conjunctivitis adenoviruses types 3 and 7 have been encountered. The etiology of epidemic keratoconjunctivitis is of great practical interest since the infection is often spread by ophthalmologic procedures, e.g., tonometry. As to the properties of these agents, we know that they are resistant to all known antibiotics. They pass filters which hold back bacteria and they are resistant to ether. Thermal inactivation occurs in 30 minutes at 56° C.

O. Vivell

German Med. Month., 1957, *2:* 122

THE LIDS

OPERATION FOR LAGOPHTHALMUS ACCORDING TO LEXER-ROSENTHAL'S TECHNIQUE

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Klin. Monatsbl. Augenh., 1957, *130:* 1–7

Disfiguration, troublesome lacrimation and threat to the cornea form the unpleasant triad associated with lagophthalmus.

Five men between the ages of 42 and 63 with lagophthalmus resulting from peripheral facial paralysis causing paralysis of the orbicularis oculi muscle and occasionally of the orbicularis oris muscle were operated on according to Lexer-Rosenthal's technique, which consists of transplantation of a masseter into the area of these two paralyzed muscles. A curved cutaneous incision was made at the temple and a broad portion of the temporalis muscle was detached from its muscular insertion at the squamous portion of the temporal bone. It was split into two tips which were led to the upper and lower eyelid by way of two cutaneous tunnels. At a distance of 1 cm. lateral to the median canthus the tips were sutured internally to the skin, ½ cm. below the palpebral margin.

This plastic operation of the temporal muscle gave surprisingly good results. The lateral horizontal pull of the temporal muscle caused the canthus to be somewhat lifted up and pulled outward. At the same time the palpebral fissure became narrower. Initially it followed the masticatory movements, but soon it closed more or less simultaneously with the other eye. The missing Bell's phenomenon recurred. Electrical examination showed satisfactory excitability of the operated lids. It is difficult to say whether this is to be considered as a reaction of the implanted temporal muscle or whether new fibers of the orbicularis muscle have been again innervated. Complete closure of the eyelid occurred only in one patient and only with effort. An adequate protection of the cornea was obtained in three patients. Continued application of ointment will always be advisable. One cannot say that the appearance of the patients became inconspicuous, but their condition became functional and cosmetic and the improvement which was obtained was such that the operation should be remembered.

Comment: The technique of Lexer-Rosenthal for transplanting temporalis muscle to the eyelids for lagophthalmus may not be too well known to ophthalmologists on this continent. This reviewer has never seen a patient upon whom this operation has been performed. It is, therefore, of considerable interest to read of five patients with lagophthal-

mus to whom the operation was beneficial. Alternative measures for the protection of the cornea, namely tarsorrhaphy, protective goggles and application of ointments, do not offer the cosmetic advantages of muscle transplantation, and this method would seem worthy of more extensive trial.

HUGH L. ORMSBY

CARCINOMA OF EYELIDS AND CANTHAL REGION

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Geriatrics, 1957, *12:* 181–184

Carcinoma of the eyelids is invasive and may result in death even when it does not metastasize. The carcinomatous nature of the tumor can usually be recognized by its gross appearance as an ulcer with raised edges or by the history of a hard solid mass that has been present in the eyelid for several weeks. As in the case of other tumors, however, the diagnosis must be confirmed by biopsy and microscopic examination. If the tumor is small, it may be removed by excisional biopsy, making further treatment unnecessary. In general, treatment, to be adequate, must consist of removal of the malignant tumor, either by excision or irradiation, and the prevention of any later breakdown; protection of the eye; and repair of the deformity caused by the removal of the tumor. Spontaneous reconstruction after excision sometimes makes secondary repair unnecessary. In many cases, however, immediate reparative action must be taken to protect the eye if it is to be saved. Repair procedures are no less necessary after eradication of the tumor by roentgenographic treatment than they are after excision, but the work of reconstruction is much more difficult when the tissues have been irradiated. Simple methods of reconstruction, utilizing the unaffected eyelid and as much of the other as remains after excision of the tumor, are sometimes preferable to flap reconstruction of the lids, because lids reconstructed by the use of a flap are essentially akinetic, even when the tissues used are derived from adjacent areas. Exceptionally severe cases in which exenteration of the orbital contents has been required may have to be treated by blanking out of the orbital region.

Although basal cell carcinoma, the type usually found in the eyelid region, may not metastasize as such, it constitutes a threat to life because of its invasive character. Usually neither the size nor the microscopic appearance and interpretation of these tumors provides any clue to their future behavior. Extension may involve the eyelids, the orbit, or the ethmoid cells, and continue intracranially. "Field fire" basal cell carcinoma may involve the eyelids and, because of the

apparently healed center, its actual extent may be misjudged. Grossly, this tumor has a smooth, finely rolled edge surrounding the flat center portion. Activity seems to progress outward from the edge, but, on microscopic examination, active tumor elements are also detectable in the apparently healed center.

Squamous cell carcinoma occurs less often in the upper part of the face, but it is not uncommon. It usually appears as an ulcer, and microscopic examination may be needed to distinguish it from basal cell carcinoma. Metastases, usually first to the neck, are not infrequent. Melanoma involving an eyelid is characteristically pigmented and easily diagnosed, but the usual microscopic examination should be made for confirmation. Malignant tumors arising from other elements in the eyelids are less common and can usually be identified only after protracted microscopic study. Finally, carcinoma of the eyelid may arise from a mixed tumor of the lacrimal gland, or it may represent extension into the eyelids from contiguous structures or metastasis from other areas.

Carcinoma involving the puncta or lacrimal duct system usually requires excision, because irradiation adequate for permanent control causes scarring and constriction extensive enough to obstruct and prevent tear collection. Surgical treatment may also be needed after irradiation of the eyelids or the canthal regions because of persistence or recurrence of the malignant tumor, or as a result of the natural retraction of the eyelids during healing, because carcinoma sometimes develops later as a sequel of the irradiation. Chronic irradiation dermitis of the eyelids is seen frequently, and must be treated by an operation that includes removal and replacement with a free graft if the certain development of carcinoma is to be prevented.

The area of potential metastatic spread should be included when eyelid tumors such as squamous cell carcinoma and melanoma are treated. Removal of the primary tumor and the cervical lymph nodes in continuity if possible is desirable, especially if metastases are already present. In any case, every patient with an eyelid tumor capable of metastasizing is a candidate for neck dissection, and when dissection is decided on, it should be complete, including removal of the sternomastoid muscle and the jugular vein.

Comment: In the practice of ophthalmology, one so seldom sees malignancies of the eyelids that the potentialities of some of these tumors for metastasis and death may be forgotten. The important group of meibomian gland tumors, recently reviewed in the Survey of Ophthalmology (Straatsma, 1956, *1:* 554), has unfortunately been overlooked in this article. Nevertheless, there is much information of value presented.

The authors apparently prefer the surgical removal of lid tumors, followed by irradiation if necessary. This is a safe procedure, but leads frequently to cosmetic problems which one may try to avoid by advising irradiation as a primary procedure. The authors point out that carcinoma may develop later from the irradiation, and surgery is not easy to carry out in such devitalized tissues.

Neck dissection for squamous cell carcinoma and melanoma of the lids, removing the neck nodes and sternomastoid muscle, seems drastic. It behooves us, as ophthalmologists who may see these lesions in the early stages, to advise treatment early, in order to avoid such extensive and disfiguring surgery.

HUGH L. ORMSBY

SYNKINETIC LID RETRACTION

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Brit. J. Ophth., 1957, *41:* 247–253

Abnormal retraction of the upper eyelid in congenital ptosis and acquired oculomotor ophthalmoplegia in the phase of its recovery is apparently more common than the literature suggests. Several different types of this disorder were present in nine patients reported on by the author, three of whom had abnormal lid retraction of more than one variety. Paradoxical lid retraction on occlusion of the sound eye was congenital in two patients and acquired in two others, in one of whom it was due to typhoid and in the other to a head injury. Fuchs' phenomenon of retraction on attempted adduction was present in four patients; in one it was congenital and in the other three it had resulted from subarachnoid hemorrhage, typhoid, and head injury, respectively. The same phenomenon was also exhibited on attempted abduction in one patient who had ophthalmoplegia resulting from syphilis.

The pseudo-Graefe phenomenon was not seen as a congenital lesion, but it did occur in two patients as a result of subarachnoid hemorrhage in one and a head injury in the other. The Marcus Gunn phenomenon, Duane's retraction syndrome, and myasthenia gravis were also seen as single entities.

The findings in one patient, a 12-year-old boy, are especially interesting because the patient had a combination of Fuchs' phenomenon and the pseudo-Graefe phenomenon, with paradoxical lid retraction on occlusion of the sound eye. The boy, who was first seen on August 2, 1956, had sustained an injury to the right side of his head at the age of five years by falling onto a hard floor from a height of 16 feet. On regaining consciousness after three days, he was discovered to have ptosis of the right upper eyelid and incomplete movements of the eyeball in all directions. In the following three months, a certain degree of improvement took place, but thereafter the condition remained unchanged. There was ptosis on the right side in the primary position. On occlusion of the left eye there was paradoxical lid retraction. On looking to the right, the ptosis increased. Elevation of the right globe was absent and the eye was slightly abducted. Adduction of the right eye was absent, and when it was tested, a retraction of the right lid was seen. The pseudo-Graefe phenomenon of lid retraction was present on downward movement of the eyeball. The left eye was normal in all respects. In the right eye, vision was reduced to counting fingers at a distance of 2 m.; the optic disk was normal; and the pupil was completely paralyzed. This unusual combination does not appear to have been previously reported in the literature.

Comment: Jain has done ophthalmology a service in recording nine patients with various types of abnormal lid retraction. Ophthalmologists interested in neurology will find some

of the case histories worthy of close study, since the mechanism of retraction following typhoid fever and subarachnoid hemorrhage is difficult to explain. The frequency of Fuchs' phenomenon of retraction on attempted adduction (four patients) in this series, only one of which was congenital, is surprising. Patients with these lesions are seldom encountered in office and clinic practice, and reports in the literature are scanty, so that it is well to have these conditions reemphasized from time to time in the literature by reports of this type.

HUGH L. ORMSBY

THE GLOBE

EVISCERATION WITH RETENTION OF THE CORNEA

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Tr. Am. Ophth. Soc., 1956, *54:* 349–355

Since the time of the first enucleation, ophthalmic surgeons have tried to replace the eye with some form of prosthesis that will give the patient a natural appearance. They have found that, for the best results, two things are necessary: the replacement of orbital volume and the placing of a shell or plastic eye in the socket. However, the problems of fixed stare and the lack of ocular movement have always been the severest handicaps in the use of any sphere within Tenon's capsule, or of any other appliance that does not move with the fellow eye and that does not fill out the socket.

The best match for an eye is the fellow eye. In the procedure of evisceration with retention of the cornea described by the author, the volume of the affected eye can be kept close to its normal total and the amount unavoidably lost can be replaced with a shell placed as a contact lens type of cover over the front of the eviscerated eye. This method has been used successfully in 95 per cent of more than 200 patients. It is a straightforward, logical surgical procedure that can be carried out in almost every instance without complication and without difficulty.

The two main contraindications for evisceration are, first, the presence of a tumor within the globe and, second, the possibility of causing sympathetic ophthalmia, which would be extremely serious. The complication of tumor within the orbit was encountered in two of the patients, one of whom was a woman who had had uveitis and who asked to have her eye eviscerated for appearance's sake. During the operation, a melanoma was discovered and the eye had to be enucleated. She has had no further complications. Sympathetic ophthalmia, the second main contraindication, has never been encountered, nor even any condition remotely resembling it.

The surgical procedure is not a difficult one. An incision is made from 9 o'clock to 3 o'clock through the conjunctiva; then, with a cataract knife, the sclera is incised throughout the extent of the incision, nearly 180 degrees. The incisions are approximately between 8 and 10 mm. from the margin of the cornea, anterior to the superior rectus muscle. Picking up the margins of the wound, fixing three or four hemostats, separating the wound, and then, with a forceps wrapped in gauze, removing the contents of the orbit is the next procedure. Special care must be taken to remove every shred of the uvea, to avoid sympathetic ophthalmia. The globe can be everted, and hemorrhage can be stopped by cautery; the inside of the eye is then wiped out with an applicator impregnated with iodine, after which it is irrigated with alcohol and, finally, with saline. An 18 or 19 polyethylene or KLF sphere is then inserted inside the scleral shell. A satisfactory result can be obtained with either a plain polyethylene sphere or a mesh covered ball. Whichever type is used, however, the ball should not be too large, because if it is, it will stretch the sclera and then, if hemorrhage should increase the pressure of the eye, the wound might open. On the other hand, since the main problem in evisceration is to replace volume, an 11 mm. sphere is the smallest that should be used in almost every instance, and it is possible to go as high as a 20 mm. ball in an old buphthalmic globe. It is not necessary to place a conformer in the socket; as a matter of fact, it is wiser not to, as a pressure point may later be established, if subsequent edema makes the eye very hard.

When the ball is in place, the scleral wound is sewn together with a double armed 3-0 catgut suture at 12 o'clock. Then one arm of this suture is used to close the wound to 9 o'clock and the other is used to close it to 3 o'clock. The stitches should be locked as the closing proceeds. When the sclera is closed, the arms of the suture are brought up through the conjunctiva and are used to close it in the reverse direction until, at 12 o'clock, they meet and are tied together. The lids are sewn together, preferably with two interrupted sutures, and the edema is reduced by means of an iced glove or cold compresses. In questionable cases, antibiotics should be given before the operation and should be continued for several days after it. Antihistaminics may also be given to lower the incidence of edema and reaction.

The reaction is sometimes quite severe. The lower conjunctiva becomes edematous, and the eye becomes quite firm and sometimes painful. The pain, which is usually controlled by sedatives though Demerol is sometimes needed, may persist for several weeks, especially if the lid sutures do not hold. Similarly, the edema and conjunctival reaction may last as long as a month. In general, the complications have been those of discomfort rather than of infection or of extrusion of any of the spheres.

The most difficult part of the entire procedure is that of fitting the shell, which must be fitted in the manner of a contact lens and which is therefore called a contact shell. Frequently, an impression of the eye and socket is made to insure a perfect fitting. There can be no pressure points on the cornea; otherwise the cornea or sclera may rub through or erode. This is especially likely to happen during the early postsurgical months. Mucus has not been one of the

serious complications of this procedure, but, when it appears, one can put a small hole through the shell similar to the lacril-hole of a contact lens. This will make it possible to cleanse the posterior part of the shell with a DeVilbiss spray or some similar apparatus. Infection was never encountered in connection with this operation.

Evisceration with retention of the cornea is a procedure that offers many advantages. The entire eye does not need to be removed, and the patient is therefore not so seriously injured psychologically. The eye is in its proper position in the socket, and it has simultaneous movement with its fellow. The extent of the movement is the greatest that can be obtained. In most instances there is little or no drainage and there is practically no sulcus in the upper lid. The procedure can be carried out successfully in almost 99 per cent of all cases and it should be used as a primary procedure in eyes badly traumatized in industry.

Comment: Ideas concerning the dangers of evisceration have been so firmly implanted in the minds of most ophthalmologists that widespread acceptance of this procedure may come rather slowly. As McLean pointed out in his discussion of Ruedemann's paper, the risk of sympathetic ophthalmia is small and yet it is present. I can imagine that should one have a patient who developed this complication, one case would be sufficient to prejudice the ophthalmologist permanently against the operation.

Final decision as to the type of operation might well depend on the individual case, a fact which has possibly not received the attention it deserves. In a patient with deep set eyes and overhanging brow, a simple enucleation frequently gives an excellent cosmetic result. On the other hand, a patient with prominent eyes may achieve a much more satisfactory result if a procedure such as Ruedemann describes is carried out.

DANIEL SNYDACKER

THE LENS

MEGALOCORNEA AND CATARACT

IVAN STANKOVIÉ AND ZLATIMIR KECMANOVIÉ

The Ophthalmological Clinic of the Faculty of Medicine of Belgrade, Jugoslavia

Ann. ocul., 1957, *190:* 36–42

In considering the association of megalocornea and cataract, some of the characteristics that distinguish megalocornea from glaucoma may well be recalled. These are, first, the fact that it is generally bilateral and that it occurs oftenest in men (93 per cent of the patients in the cases published so far have been males). The essential feature of the condition is the diameter of the cornea, which ranges from 12.5 to 18 mm. The cornea itself is transparent; Descemet's membrane is not ruptured; and the corneal curvature is not appreciably altered. Embryotoxon, with conservation of the normal structure of the limbus, is often present. A deep anterior chamber is also characteristic of megalocornea, but the sclera, the iris, the lens, and the fundus remain normal, as does the visual acuity. The intraocular tension is never increased. The condition is clearly a hereditary, sex linked anomaly, carried by females and appearing in males as a result of recessive transmission. It is less rare than it is sometimes thought to be. Duke-Elder in 1943 stated that there were about 80 reports on megalocornea in the literature, and the present authors have been following a series of cases at the Ophthalmological Clinic in Belgrade for several years.

Cataract is a frequent complication of megalocornea, but the number of cases in which operative removal has been reported is surprisingly small—only 30. Analysis of the data presented in the reports shows that the results obtained in the period from 1888, when the first operation was performed, to 1931 were mediocre: only 65 per cent of the operations were successful, and loss of the vitreous occurred in about 40 per cent. The results obtained from 1931 to 1955 were much better, with success being achieved in 90 per cent. From their own experience in two cases, the authors believe that the surgical removal of cataract in patients with megalocornea is not a particularly complicated procedure. The most important thing seems to be the position of the incision in the cornea. In their own patients, the authors placed the incision in the limbus as close to the cornea as possible. The next step, which is also important, is the placing of stay sutures in the cornea and the perfect coaptation of the wound after the extraction. The intracapsular method of extraction, which they used, seems to them to be the easier, because they had no difficulty in removing the lens. Stress must also be laid on the introduction of air into the anterior chamber, by which its reformation is assured. The use of this technique in their patients produced favorable results, with no complications either during or after the operation. It seems, therefore, that cataract surgery presents no special danger in patients

with megalocornea. The number of cataract operations performed in such patients very probably exceeds the number that have been reported. Consequently, if Smillie's suggestion (1955) that every case in which a cataract operation is performed in a patient with megalocornea should be reported is followed, it will undoubtedly help to correct the adverse opinion now mistakenly held on this subject.

Comment: The reviewer has not had occasion to operate on a patient with megalocornea. The authors' suggestion that the section be corneal seems valid. One would certainly want additional sutures because of the large cornea.

P. Robb McDonald

CONTRIBUTION TO SO-CALLED EXFOLIATION OF THE ANTERIOR CAPSULE OF THE LENS

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Ophthalmologica, 1957, *133:* 309–320

Between 1918 and 1938, Vogt and his pupils published many papers concerning so-called exfoliation of the anterior lens capsule. Vogt believed that the microscopic appearance of this condition resulted from degenerative changes in the anterior capsule, causing the typical morphologic picture with fragments and crumbs deposited on the iris and on the posterior surface of the cornea. Busacca, however, believed that the well known changes depend on deposits on the capsule of the lens.

Landolt reexamined the 35 cases in which the microscopic findings were reported by Vogt and reevaluated the changes observed in 18 eyes obtained from 11 patients. In 13 eyes the capsule of the lens showed definite changes as described by Vogt, thickening, formation of vacuoles and lamellar structure. These changes occurred only in the anterior capsule and most frequently in the pupillary area. In 6 of the 13 bulbs these changes were the only ones observed, while in the remaining 7 eyes there were in addition changes of an appearance similar to that of bushes of a hedge along a field path, as described by Busacca. In 5 eyes the capsule of the lens did not show unequivocal changes.

The lens which had been removed from a 74 year old man with the clinical diagnosis of exfoliation of the capsular membrane of the lens was examined microscopically by the author. A section from the anterior capsule of the lens in the area of the zonular fibers showed typical Busacca's deposits when Masson's trichromic stain was used. The deposits were free from cell elements and consisted of fine granules and seemed to be related to hyaline or to a similar protein

substance. A section of the anterior capsule of the lens in the pupillary area indicated an irregular membrane on the anterior capsule when Mallory's stain was used; Busacca's deposits were not visible, and the capsule itself was unimpaired and normal. The interpretation of these findings is difficult because the typical Busacca's deposits are certainly not artifacts. They represent the substrate of the pathologic changes associated with so-called exfoliation. It is typical that they are found predominantly in the median and outer peripbery of the anterior surface of the lens, corresponding with the clinical findings, while they are rare in the pupillary area. They are clearly deposits on the capsule of the lens. It would be most peculiar if crumbs of the capsule of the lens on the anterior surface of the lens would always assume such unusual forms. It would be likewise peculiar if these formations which have the same appearance throughout would represent fragments of the capsule of the lens which had been deposited on the posterior surface of the iris, while on the anterior surface of the lens they should correspond with exfoliative parts of the capsule of the lens. Finally they are absent in the anterior chamber, where they must have occurred if they had originated from the anterior capsule of the lens, corresponding with the current of the aqueous humor of the eye.

One is tempted to consider so-called exfoliation as a special syndrome in which besides these well known morphologic changes in the area of the posterior chamber, additional symptoms occur as follows: increased washing out of uveal pigment (already mentioned by Vogt), considerably increased permeability for fluorescein in the anterior uvea (mentioned by Sampaolesi last year), and degeneration of vitreous body (Sugar, Irvine). The cause and pathogenesis of this disease still require further elucidation. The patients are predominantly men of advanced age. Cataract is not always present. It might be possible that histochemical analysis of the aqueous humor may clarify these problems.

There are two interpretations of the pathologic changes in the area of the capsule of the lens which do not have the appearance of the typical Busacca's deposits: (1) They may be considered as proper degeneration of the capsule of the lens according to Vogt, but the question remains to be answered whether one is dealing with parts of the capsule itself or with parts of the pericapsular membrane. (2) It is more probable that the changes in the capsule of the lens may not be changes in the capsule in Vogt's sense, but may be deposits on the capsule of the lens which as such may be normal. In favor of this intepretation is the fact that so frequently Busacca's deposits could be found simultaneously with changes of the capsule of the lens (12 of 18 eyes). Histologic findings also support this interpretation. In a microphotograph of the left eye of an 87 year old man one sees a clear line of separation within the thickened capsule, which may easily be considered as the borderline between the real capsule of the lens and homogenous material which had been deposited and which stained darker. In a second microphotograph, also taken from Vogt's specimens, a small pigment clod is found within the capsule of the lens, as well as fine vacuoles and so-called branching off lamellae. How could pigment come into the capsule of the lens? The most unequivocal explanation is that this pigment had been de-

posited with the other material on the capsule of the lens and that it marked by its position the surface of the real capsule of the lens.

Among these deposits in the pupillary areas the histologic appearance may vary, and Vogt has described it very strikingly as lamellar structure, vacuolar degeneration, and lamellar splitting. This provides an anatomicopathologic explanation for the peculiar appearance of the anterior surface of the lens in the pupillary area, where frequently a real felt is missing and only a disk or a membrane may be found on the capsule. The clinical records of four cases in which only typical changes of the capsule of the lens could be demonstrated revealed that pupillary border felt and peripheral felt were absent throughout and that only a disklike deposit was found in the center of the anterior surface of the lens. One is therefore tempted to consider a related but not identical disease aspect, in which only one part of the clinical and anatomicopathologic changes of the symptoms of exfoliation occurs.

In reality, the changes of the capsule which do not have the appearance of the typical Busacca's deposits may represent deposits on the capsule of the lens in the pupillary area. They must be interpreted in the same way as the typical Busacca's deposits and they belong to the disease aspect of the so-called exfoliation, a term which should be replaced by a better one.

Comment: This article is essentially the same as that reviewed in Survey of Ophth. 1956, *1:* 537. The author has reviewed Vogt's specimens and has decided that in the majority of the cases they are deposits on the anterior lens capsule. The author agrees that the concept of exfoliation of the lens capsule must be dismissed as a clinical entity, and that the so-called exfoliation is essentially a deposit on the anterior lens capsule.

P. Robb McDonald

THE INTRAOCULAR PRESSURE

GONIOSCOPY IN PRIMARY GLAUCOMA

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Tr. Ophth. Soc. Australia, 1956, *16:* 13–28

Simple glaucoma and closed angle glaucoma are two completely different and entirely independent clinical entities. Although they are accompanied by the same symptom, ocular hypertension, they have nothing else in common and they should never be studied together. Differentiation between them is not difficult in the case of inflammatory closed angle glaucoma, either acute or subacute. Noninflammatory or chronic closed angle glaucoma, however, can easily be confused with simple glaucoma. To avoid this confusion, gonioscopy is not merely important, but actually necessary.

According to Barkan (1936), two varieties of glaucoma can be distinguished —wide angle glaucoma and narrow angle glaucoma. In wide angle glaucoma, the opening of the angle is large or medium, the depth of the anterior chamber is normal, and the goniosynechiae form later. In narrow angle glaucoma, on the other hand, the opening of the angle is narrow, the anterior chamber is less deep and the goniosynechiae form early. Thus, for Barkan, only the degree of the opening of the angle is important.

By contrast, for Goldmann (1941)—and his opinion is shared by the author—the degree of opening of the angle is of no importance and the only significant fact to be ascertained is whether, during the period of raised ocular tension, the angle is open or closed. If it is open, even though it may be narrow, the condition is one of simple glaucoma. If, on the other hand, it is closed during the hypertensive period, even though it may be wide when the tension is normalized, the condition is one of congestive glaucoma. The narrowness of the angle does not in itself necessarily constitute a predisposition towards congestive glaucoma; this predisposition may not be presumed to exist unless the angle is really blocked by the iris during the hypertensive crisis.

In simple glaucoma the angle is generally open and free, even though more or less permanent ocular hypertension is present. Furthermore, in differentiating between simple glaucoma and closed angle glaucoma, stress must be placed on the following facts: (1) No matter to what degree the angle is open, no matter what the level of ocular hypertension, and even when the tension curve is at its highest, the angle in simple glaucoma remains open and the iris never adheres to the scleral trabeculum as in closed angle glaucoma; and (2) the goniosynechiae, which form rapidly and easily in closed angle glaucoma, are exceptional and always very late in forming in simple glaucoma. Even though most of the angles are large or medium, narrow angles may also be found, as in closed angle glau-

coma or as in normal subjects (over 50 years of age). The degree of the opening of the angle may well be variable, according to the refraction (i.e., greater in myopia and lesser in hypermetropia), according to the size and the position, more or less anterior, of the lens (this explains the fact that it diminishes after the age of 50), and according to certain individual anatomic conditions. No relationship exists between the degree of the angle opening and the rate of ocular hypertension.

Simple glaucoma is not influenced by the mydriatics which do not provoke hypertension and may be instilled without danger, except in the rare cases in which the narrowness of the angle may bring with it a blockage by the root of the iris. Pilocarpine also produces no appreciable gonioscopic change. The author's observations in 200 cases of simple glaucoma seem to warrant the following conclusions: (1) There is no gonioscopic sign that is pathognomonic of simple glaucoma; (2) pronounced modifications may be found, but they differ in no way from those sometimes found in normal subjects beyond middle age; (3) the degree of opening of the angle is of no special significance; (4) obvious sclerosis of the scleral trabeculum was not seen, but a feltish or woolly appearance of the ciliary band was observed in 11 per cent of the cases (normal percentage, 4 per cent); (5) pigmentation of the scleral trabeculum or of the canal of Schlemm is no more frequent in glaucomatous eyes than in normal eyes of persons over 50 years of age; and (6) blood is normally absent from the canal of Schlemm in the eyes of patients with simple glaucoma.

These findings show that in simple glaucoma even the most minute gonioscopic examination fails to reveal any specific morphologic changes indicating increased resistance to the flow of aqueous. Consequently, it is not possible to diagnose simple glaucoma merely by examination of the angle. The exact nature of the obstacle responsible for the increased resistance to the flow of the aqueous, to which simple chronic glaucoma is admittedly due, is not known, nor has its precise location been determined. Conceivably, it may be either a mechanical obstruction, an alteration of the vascular wall, or a vasomotor phenomenon.

In general, in congestive glaucoma, it may be said that closure of the angle precedes the elevation of the tension. Closure, then, is the cause of the hypertension and it is also concomitant with a considerable elevation of resistance to the flow of the aqueous. As soon as the pupil contracts under the influence of miotics, the angle opens, though remaining very narrow, and the ocular tension becomes normal again. If miotics are suspended, the pupil redilates, the angle progressively closes, and the tension rises rapidly again. These facts show that the ocular hypertension appears only at the moment when the angle closes. In certain exceptional cases, however, the angle is not completely closed even during the period of hypertension. Gonioscopic studies made after the congestive crisis show that at the beginning of a chronic congestive glaucoma or after mild and fleeting attacks, the angle may remain completely free. If the congestive crisis lasts for 24 hours, partial goniosynechiae, which may break again, at least partly under the action of miotics, are formed. But if the crisis is prolonged for more than two or three days, if it is repeated, or if it is very acute, the inflammatory reaction that

accompanies it will lead to the formation of definite goniosynechiae which persist and are so numerous that solid annular synechiae may appear. It therefore follows that (1) the goniosynechiae formed as the result of a hypertensive crisis prevent a return to normal; (2) the presence of an established annular goniosynechia renders miotics inoperative; and (3) a congestive crisis should be treated at once by the use of miotics, or, if these are ineffective, by an operation, if the formation of goniosynechiae with all their consequences is to be avoided.

The gonioscopic findings in 61 patients with congestive glaucoma studied by the author show that the sudden rise in ocular tension in this condition is due to the abrupt and total blockage of the angle by the root of the iris. As long as an opening remains, however narrow it may be, flow of the aqueous is possible and the tension does not rise. Narrowness of the angle undoubtedly makes it easier to block, yet it cannot be considered indispensable to blocking. Congestive glaucoma may appear in an eye with a medium angle or in a myopic eye with a large angle, and, on the other hand, an eye with a narrow angle may never be affected by congestive glaucoma. Even though blockage of the angle by the iris occurs at the beginning of the rise in ocular tension, and though it is facilitated by narrowness of the angle, the blockage itself is not the primary cause of the congestive crisis but rather its result. The primary cause, in fact, is probably a neurovascular element that is still undetermined. In general, in congestive glaucoma, the hypertension is secondary and the true cause, which is the neurovascular one, probably lies outside the eye at the level of the diencephalon and consists of an edema of all parts of the ocular globe. This edema leads, first, to the closure of the angle and, later, to the increase in tension. Understandably, then, closed angle glaucoma usually appears only in persons with a particular neuropsychic temperament that is characterized by emotionalism, anxiety, and hypersensitivity.

Comment: In reading this paper, one must think back to the lectures of Duke-Elder in Los Angeles in 1952 in which he stated that the narrow angle only *follows* repeated attacks of congestion and mild rises of tension which at first are without angle narrowness, and that although congestive glaucoma is usually characterized by narrowness of the angle, a typical attack may occur without such narrowness.

François follows this earlier view of Duke-Elder since he states that, although narrowness of the angle makes it easier to block, it cannot be indispensable to blocking. He considers the block to be a result of the congestive crisis, not its cause, which he considers neurovascular.

North American ophthalmologists, as a group, do not concur in this viewpoint and consider angle closure glaucoma to occur only in predisposed individuals and block of most if not all of the angle to lead to tension rise. Although no denial is made of the importance of neurovascular factors, it is considered that these are the remote precipitating factors only.

The absence of comment on pupil block by this outstanding investigator and teacher is notable.

H. Saul Sugar

THE FELLOW EYE IN ACUTE CLOSED ANGLE GLAUCOMA

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Glaucoma Clinic, Institute of Ophthalmology, University of London, London, England

Brit. J. Ophth., 1957, *41:* 193–199

Investigation of a series of more than 3,000 cases of glaucoma of all types at the Glaucoma Clinic of the Institute of Ophthalmology has shown that miotic treatment is no sure guard against the occurrence of an acute attack in the second eye. A patient on miotic therapy may be relieved of his symptoms, for example, by pilocarpine 1 per cent thrice daily and yet may have a pathologic rise of tension under provocative tests. Such a person is therefore in an unsafe position; he may have an acute attack in this eye in a moment of vasomotor instability, or he may come to have chronic closed angle glaucoma with eventual peripheral anterior synechiae and cupping of the optic disk. A plea for peripheral iridectomy as a treatment for very early closed angle glaucoma and as a prophylactic measure has been made in recent years by various authors, and the indications and contra-indications for this relatively simple procedure have been clearly defined.

In order to establish a basis on which to assess the treatment of the fellow eye, a study has been made of 200 patients with acute unilateral closed angle glaucoma. Excluding 7 patients who had undergone a prophylactic operation, it was found that symptoms developed in the other eye in 102 patients (53 per cent). In 35 per cent the symptoms comprised another acute attack. The prognosis for the second eye may be summarized as follows: (1) The fellow eye may not be glaucomatous and in a few cases may never become so, but this can only be determined by constant surveillance. If the eye is not going to become glaucomatous, the instillation of miotics is a waste of time, but to assert this in a given case would be hazardous. (2) The eye may become glaucomatous at a later date, as did most of those in this series. Miotics are not a sure guard against this development, and in 29 cases they did not even prevent a second acute attack. In 25 other cases symptoms of chronic angle closure have set in in spite of miotic treatment; many of these cases are apparently being controlled on stronger doses of miotics, but how long they will remain so, only time will tell. It seems likely that if these patients live long enough they will either exhibit cupping of the disk as a result of impaired filtration, or will suffer the crisis of an acute or subacute attack. (3) The eye may have incipient glaucoma as shown by symptoms of pain, blurred vision, and halos, or by a positive response to provocative tests. Many of the patients with a positive response to such tests have noticed no symptoms and are fortunate to have had their trouble discovered by the tests. If a completely reliable test were available, many more patients would almost certainly be found to have glaucoma. (4) The eye may be undergoing an acute or subacute attack when the patient is first seen.

Provocative tests should, therefore, be applied to the second eye even when

it seems to be clinically normal. Tests of this kind are also helpful in determining whether a manifest chronic closed angle glaucoma may be partially controlled by a miotic at any given time.

Peripheral iridectomy is apparently a safer guard against trouble than miotic therapy, at any rate in younger patients and in those whose occupations take them away from surveillance for long periods. The operation is subject to fewer complications than any other glaucoma procedure. Properly done, it should check the progress of peripheral iris bombé, peripheral anterior synechiae, and trabecular blockage, which lead eventually to cupping of the disk and may at any time be interrupted by an acute attack.

Comment: Bain has emphatically emphasized the findings of Winter, who found that even when miotics are used continuously, about 40 per cent of patients with angle closure glaucoma have a second attack in the fellow eye. Where miotics were used intermittently or not at all, 89 per cent of 27 patients suffered an attack in the second eye within five years of the first attack in the first eye.

There is a danger in the conclusion of the author that there is no significant difference in time before involvement of the second eye between patients treated with miotics and those who did not have treatment. This might lead to the giving up of miotics in such cases by some ophthalmologists. This is probably not a valid conclusion since miotics have, in many cases with repeated attacks, led to complete normalization of tension and the absence of symptoms or signs for many years. Thus, the use of miotics cannot be considered a waste of time. This editor does not believe that these patients without evidence of glaucoma will develop chronic angle closure glaucoma, which is relatively uncommon. The high number of chronic angle closure cases (25) suggests that Bain may be including some cases of simple glaucoma, possibly with shallow chambers, in his series. Nor does the fact that a provocative test is positive mean that the previous uninvolved eye will necessarily develop angle closure. It means only that this is potentially so and may become involved if the proper combination of precipitating factors are present.

The suggestion that peripheral iridectomy is a safer guard than miotics is unquestionably true, but not all patients permit surgery on the second eye, and it is not true that this operation is absolutely complication free.

H. Saul Sugar

THE CHOROID AND RETINA

DETACHMENT OF THE CHOROID (SPONGIOSIS CHORIOIDEAE)

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Klin. Monatsbl. Augenh., 1957, *130:* 347–371.

Detachment of the choroid may be found most frequently in patients of advanced age and in those with high intraocular pressure. In contrast to the detachment of the retina, the detachment of the choroid is not caused by a free fluid but by an edematous thickening of the choroid which is frequently associated with actual fluid cavities. The term "spongiosis chorioideae" seems to be most suitable since it corresponds with the morphologic appearance and the pathogenesis of these changes. The term "detachment of the choroid" originates from an erroneous morphologic concept. Instead of free retrochoroidal fluid which one may expect in the presence of a true detachment of the choroid, puncture of the choroid fluid will frequently yield a small amount of fluid only and the recognizable choroid appears to be of glassy edematous type. If one increases and deepens the incision or if larger vesicular cavities are present, one may obtain a larger amount of fluid by puncture (0.5 cc. or more) from the edematous choroid; this amount of fluid corresponds with the loss of fluid associated with a scarified edema or a bulla, respectively. Microscopic examination of human eyes with perforated lesions, with fistula formation or with chronic iridocyclitis or microscopic examination of eyes of rabbits in which the so-called detachment of the choroid had been produced artificially, revealed the presence of edema of the choroid and not a detachment of the choroid by free fluid.

According to its course, three types of the so-called detachment of the choroid may be distinguished.

(*1*) *Choroid Detachment with a Shallow Anterior Chamber.* This occurs within two to seven days after intraocular operations in the anterior portion of the bulbus, and most frequently after fistulizing operations for glaucoma such as Elliot's trephining and iridencleisis, but also after operations for cataract and after perforating injuries. It may be associated with a chemosis of the conjunctiva and with abolition of the anterior chamber. Both the abolition of the anterior chamber and the detachment of the choroid are partly related to the outflow of the aqueous fluid outward or below the conjunctiva, but this outflow of the aqueous fluid of the eye is not the only cause of the abolition of the anterior chamber. It is possible that less aqueous may be secreted because of the reduced local blood pressure in the area of the ciliary body, and that the aqueous (as well as the vitreous) humor is shifted in the direction to the higher colloid osmotic pressure of the tissues which are depolarized as a result of change in the vegetative stimulus. An attempt at drainage of fluid from the choroid may be harmful

to the eye. Puncture of the sclera may be considered as a "second trauma" which may make the vascular condition worse instead of relieving it. The physiologic stimulus of normal movements seems to exert a somewhat normalizing influence, and it is therefore advisable for the patient to be out of bed.

(*2*) *Detachment of the Choroid with Deep Anterior Chamber* (*After Injury to the Vitreous Body*). Detachment of the choroid may occur in diseases or surgical intervention associated with changes in the posterior portion of the bulbus, such as detachment of the retina or operation for this condition, fistula of the posterior globe and any injury to the vitreous body or loss of vitreous. The clinical picture is that of a deep anterior chamber with moderate to severe exudation of albumin as the predominant feature. The depth of the anterior chamber may reach 6 mm. or more, and the lens, therefore, appears almost sunken posteriorly. This means that the space of the vitreous has been reduced and that the hypotonia (in the presence of the reduced space) may depend on a pronounced reduction of fluid. This reduction of fluid may be interpreted as a more pronounced absorption and as a reduced secretion of vitreous fluid by the retina and uvea. The detachment of the choroid is elicited by a more active change in the permeability of the vascular walls, and in addition, by a more passive shifting of tissue fluid. The amost complete absence of leukocytes in the aqueous is typical. The iris is hyperemic and the clinical aspect is similar to that of so-called toxic iritis. The exudation of albumin into the aqueous fluid and the deepening of the anterior chamber regress after days or weeks despite continuation of retinal detachment or irreversible damage to the structure of the vitreous body by loss of vitreous. Experiments on rabbit's eyes showed that this type of detachment of the choroid can be produced artificially by posterior trephining. Considerable thickening and edematous swelling of the ciliary processes were also observed on microscopic examination.

(*3*) *Detachments of the Choroid in Patients with Local Diseases of the Globe.* This occurs after inflammations such as scleritis, or as a circumscribed vascular reaction. Other symptoms such as hypotonia and exudation of albumin into the anterior chamber may be absent or less marked.

Comment: The unifying concept of the pathogenesis of ammotio chorioideae in all cases as a more or less extensive hemodynamic disturbance in the uveal tract extinguishes the traditional dividing line between the postoperative type with a shallow anterior chamber and the spontaneous variety with deep anterior chamber, also known as acute hypotony. This vasomotor reaction may follow a variety of damaging influences, traumatic or toxic etc., and causes an edematous imbibition of the stroma rather than a true detachment.

The spontaneous type, produced by the author experimentally in young rabbits by injury to the posterior vitreous, was always associated with marked edema of ciliary processes and ciliary portion of the iris. This fact led to the suggestion that the main difference between the various kinds of ammotio chorioideae may be the absence or presence of anterior uveal participation in the vascular reaction.

This concept also leads to more definite ideas about therapy, at least of the postoperative type. While spontaneous regression is the rule, early ambulation of the patient is advisable if the ammotio persists for more than a few days. Lack of signs of regression

for a longer period (months) calls for closure of a fistulating postoperative scar. The "second trauma" to the hemodynamic equilibrium by the surgical procedure is preferable to the prolonged "second trauma" of continued hypotony.

No therapeutic suggestions were made regarding the spontaneous kind with notoriously poor prognosis except to refrain from removal of the subchoroidal or intrachoroidal fluid in any case of ammotio.

In the spontaneous type, great variations in the intraocular tension are occasionally encountered, varying from abnormally low to abnormally high. A diagnosis of intraocular tumor may erroneously be made if the patient is first examined during a period of increased tension, when the characteristic findings of abnormally deep chamber and iridodonesis temporarily disappear (Klien: Conditions simulating an intraocular tumor. Am. J. Ophth., *20:* 812, 1957).

It would be interesting to find out how systemic doses of acetazoleamide influence the abnormal depth of the anterior chamber which the author believes to be due to an increased production of aqueous. BERTHA A. KLIEN

NEUROLOGY

CAVERNOUS SINUS THROMBOPHLEBITIS

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Brit. J. Ophth., 1957, *41:* 228–237

Septic thrombosis of the cavernous sinus had a mortality rate of almost 100 per cent before the advent of chemotherapy and antibiotics, and even now, although the condition itself is occurring less often, the number of fatal cases is by no means negligible. Moreover, an increase in the death rate may be expected to accompany the increase in the number of penicillin resistant staphylococci.

It is important to distinguish between the varieties of cavernous sinus thrombosis, since they arise in different ways and have substantially differing prognoses. Two main groups are clearly identifiable: (1) the aseptic or "marasmic" form, which may be similar to thrombosis in the veins of the pelvis or the limbs, and (2) sinus thrombosis of septic origin. Cavernous sinus thrombosis of the second group may be infected from the start either because the site of infection is adjacent to the sinus or because the thrombus arises by septic emboli; or a thrombus that is initially free from bacteria may become infected later if the original septic condition is not overcome. The acute forms of cavernous septic thrombophlebitis that were formerly almost always fatal belong to the second group. Eagleton (1926) stated that they "present little difficulty in diagnosis; they are early accompanied by chemosis and exophthalmos, first of one eye and then of the

other, associated with profound pyaemia, and followed by death from sepsis or a complicating meningitis." This description was accurately followed by the course of the disease in two patients admitted to St. Thomas's Hospital in 1956.

In the first patient, a 24 year old woman, the infection followed the development of a sty. On admission, she was comatose with marked meningism, and reacted only to painful stimuli by purposeless movements and a high pitched cry. Her temperature (axilla) was 104.8°F., pulse was irregular, 92 per min., and respirations were 18 per min. There was severe bilateral proptosis and chemosis, the lids being so edematous that it was possible to force them apart by only 1 or 2 mm., while between them the edematous conjunctiva pouted forth. There were signs of a resolving sty on the right lower lid and the surrounding skin was hot and red. Edema extended over the upper part of the face and temples, and there was a small edematous area over each mastoid process. The pupils were visible only in part, but were central and reacted to light. No clear view of the fundi was obtained because of edema and mistiness of the refracting media. The limbs were held in flexion; the tendon reflexes were present and equal and the plantar responses flexor. Examination of other systems revealed no abnormality and the spleen was not palpable. *Staphylococcus aureus*, sensitive to streptomycin, erythromycin, aureomycin, and chloramphenicol, but resistant to penicillin, was recovered from a right conjunctival swab and from blood cultures.

Streptomycin, penicillin, and heparin were given immediatly, followed a few hours later, when the characteristics of the organism became known, by erythromycin suspension by nasal stomach tube. The streptomycin, penicillin, and heparin were discontinued on the fourteenth day, but the erythromycin was continued until the twenty-fourth day, when the temperature had been normal for a week. Local treatment to the eyes consisted of adrenaline solution (1:1000) and aureomycin cream (1 per cent) every six hours until the twenty-fourth day, and atropine 1 per cent drops daily from the seventh to the twelfth day. Tube feeding was continued until the twelfth day. She remained unconscious until the sixth day, regaining full consciousness on the twentieth day. About the sixth day, the proptosis and lid edema began to diminish on the right side. By the sixth week, they had completely disappeared, but ptosis was still substantial. By the time of her discharge from the hospital, this, too, was almost gone. Seven weeks after the onset of the illness external ocular movements were seen for the first time. Starting as a flicker, upwards in the right and lateral in the left eye, these gradually increased in range and direction until at the time of discharge six weeks later they were almost full. Both eyes had normal lateral movements, but elevation and depression were still reduced, more so on the left side. The pupils remained fixed and unequal, larger on the right side. Visual acuity in the right eye was 6/12, correctable to 6/9 and N5, and the visual field was full, but the left eye remained amaurotic. On discharge, in addition to these eye signs, she had only a minimal incoordination of the right arm and leg and slightly increased reflexes in the left leg. The cerebrospinal fluid was perfectly normal. Six months later, when she was last seen, all long tract signs had disappeared, although the pupils remained inactive and the left eye was blind. Her mental state was quite normal.

The second patient, a two week old infant delivered normally at term, was discharged from the maternity hospital as a normal baby three days before admission to St. Thomas's. Her mother, however, stated that the child had had a "bad" eye for a week. The day before admission, she had been seen in the hospital eye department and an early sty was noted in the upper lid, but no chemosis was present. The evening of the following day she became comatose and was brought at once to the hospital. Examination showed a discharging sty in the upper lid of the left eye, with moderate lid edema. The right eye was normal. Monilial infection was present in the mouth, and the spleen was enlarged. *Staphylococcus aureus* was recovered from the blood cultures. Antibiotic treatment was started but the child's condition deteriorated steadily and two days later she died.

The positive blood cultures obtained from both patients are a frequent finding, but the fact that in each case repeated cultures of the purulent cerebrospinal fluid proved to be sterile came as a surprise. A survey of 98 cases from the English and American literature since 1920 seems to show, however, that this is the usual finding. Although stys occur so often and although they were responsible for the infection in these two cases, they very rarely cause cavernous sinus thrombosis. In most (53) of the 98 cases mentioned, the original infections were furuncles of the face.

The development of penicillin resistant staphylococci makes it advisable not to rely on penicillin alone while waiting for the results of the bacteriologic studies, but to give in addition a broad spectrum antibiotic as soon as the specimens have been taken for culture. The use of anticoagulants has been questioned by some authors. On general principles, however, they appear to be fully justified and there seems to be no good reason for not using them.

In the 98 cases collected from the literature, only one of the 60 patients who recovered became blind in both eyes, and only three became blind in one eye. The cause of blindness in patients with cavernous sinus thrombosis and why it occurs in so few of them has never been satisfactorily explained. Thrombosis of the retinal veins, which might be expected, does not usually occur. Disturbance of the ocular media, such as that found in the first of the author's patients, has not previously been reported.

The development of a cerebral abscess as a complication or a postmortem finding is well recognized. Although the frontal or temporal lobes provide the more common sites, cerebellar abscesses have been reported in two cases. In the author's first patient, there was no proof of a cerebellar abscess; possibly the lesion responsible for late headache and certain other symptoms suggesting a cerebellar abscess was a thrombosis of the veins on the right cerebellar hemisphere.

Comment: Although the author points out that cases of cavernous sinus thrombosis may become more frequent as the result of the development of penicillin resistant staphylococci, he still recommends the immediate use of penicillin, a broad spectrum antibiotic, and anticoagulant therapy. Perhaps by-passing penicillin and resorting to a combination of chloramphenicol and erythromycin might be better emergency treatment, at least until the results of sensitivity studies on the organisms become available. Whether anticoagu-

lants are really helpful is difficult to determine. The author cites evidence that although dissemination of organisms might occur, the concomitant use of antibiotics makes a bacteremia less hazardous than multiple septic infarcts.

It is unfortunate that the fundi could not be seen well or followed in either case reported, and no findings could be given antedating the final occurrence of monocular optic atrophy in the case which recovered. Whether the optic nerve was involved within the cavernous sinus or whether the intense associated orbital cellulitis interfered with vascular nutrition to the nerve within the orbit cannot be answered.

One interesting observation is made in the original paper. At the time that edema first began to appear in the second eye (the important single finding which points directly to cavernous sinus thrombosis as against orbital cellulitis) a tentative diagnosis was made of penicillin sensitivity—perhaps another good reason for leaving penicillin to the syphilologists.

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OPHTHALMOLOGIC FINDINGS IN CHILDREN WITH CEREBRAL PALSY

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Pediatrics, 1957, *19:* 623–627

Recent reports calling attention to the relatively high frequency of ophthalmologic defects in children with cerebral palsy led to an ophthalmologic study of pupils attending the four special public school units for children with this condition in New York City. The children in this group were from 4 to 10 years of age; were moderately to severely disabled physically in such activities as ambulation, feeding, dressing, speech, and toilet care; and had intelligence quotients of 70 or better on serial psychometric testing. A letter was sent to the parents of each child requesting the participation of the child in the study, which was designed to answer the following questions: (1) What is the prevalence of ophthalmologic findings? (2) What types of ophthalmologic defects were found? (3) Are the ophthalmologic defects significant from the viewpoints of early case finding, the educational needs of the children, treatment, and prevention of progression of the defects? The parents were given the choice of using their regular ophthalmologic resources (private ophthalmologist or hospital eye clinic) or of using the services of the consulting ophthalmologist to the Bureau for Handicapped Children free of charge. If the former method was selected, the family's opthalmologist was asked to use a study form containing questions relating to antepartal and birth history, ophthalmologic history, and ophthalmologic findings that had

been worked out for this investigation. Forms were distributed to and returned from all 98 of the children in the special cerebral palsy classes.

Analysis of the data so obtained showed that 67 children (68 per cent) had either an ocular defect or a refractive error, or both. The most frequent type of ocular defect was that associated with external oculomotor movements (49 children); 22 of the children so affected had gross esotropia, 21 had gross exotropia, 3 had pure gaze paralysis, 1 had a ptosis of the upper lid, 1 had a fixation nystagmus not associated with any other pathologic change in the external ocular muscles, and 1 had questionable nystagmus. Two of the 22 children with esotropia had associated gaze paralysis; 2 had associated paralysis of the superior rectus (one of these also had questionable optic atrophy); 1 had associated nystagmus and optic atrophy; 2 had associated nystagmus; and 1 had questionable optic atrophy. Of the 21 children with gross exotropia, 1 had associated gaze paralysis and 1 had questionable nystagmus. Thus, although the frequency of esotropia and exotropia was practically the same, the amount of associated ocular pathologic change was much greater with esotropia than with exotropia.

The next most frequent gross ocular defect was optic atrophy. One child had almost complete optic atrophy, two others had partial, and all three had esotropia. One child had congenital cataracts and one had had enucleation for an unknown reason.

Significant refractive errors were present in 53 children (54 per cent). Complete information was lacking on 9 children. Myopia with or without astigmatism was present in 28 children; 20 had hyperopia with or without astigmatism; and 5 had mixed astigmatism. It should be noted that groups of "normal" children usually show a much lower incidence (8 per cent) of myopia than did these children.

These findings indicate the desirability of at least a routine ophthalmologic evaluation of every child with cerebral palsy. Only 20 of the 67 children with either a gross ocular defect or a refractive error or both were under the care of an ophthalmologist, and yet definite ophthalmologic recommendations were thought to be necessary for 69 children as a result of the ophthalmologic examinations.

Visual handicaps severe enough to interfere with the ability of the children to take full advantage of the educational opportunities offered them were found in 17 of the 98. Their best corrected vision was of an order usually requiring special educational methods (as in special sight conservation or Braille classes). The planning of special classes for children with cerebral palsy should take into account the special visual needs of the children, and special educational methods should be provided whenever indicated.

The need for early ophthalmologic examination and treatment is emphasized by the large number of these children who had strabismus (43, or 44 per cent). How many of the children also had associated amblyopia is not known, but since amblyopia is a frequent result of strabismus and since it can often be alleviated or prevented by adequate early treatment, the possibility that it may exist is a further compelling reason for ophthalmologic investigation of children with cerebral palsy.

Twice as many ocular defects and twice as many refractive errors were found in

the children with spastic types of cerebral palsy as in those with athetoid types. Experience with the children in this group showed that the ophthalmologic examination could usually be made with ease so long as there was no rush, no pressure, and no concern for time. Any attempt to speed up the examinations, which generally took about one hour for each child, resulted in increased tremor, decreased ability to cooperate, and increased speech difficulty, and generally made a complete examination impossible.

In all probability, children with mild physical involvement and those who are severely retarded mentally—the two groups not included in this study—should also be given an ophthalmologic examination.

OCULAR INJURIES

THE MANAGEMENT OF INTRAOCULAR FOREIGN BODIES

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Successful management of intraocular foreign bodies requires good judgment, proper equipment, and experience. The presence of an intraocular foreign body must be suspected in every case in which there is a history of hammering, shattering, or explosion. The mere presence of a foreign body in the globe, however, is no occasion for haste, excitement, and ill-advised removal. On the contrary, it is better to make haste slowly and to follow an orderly procedure. The first step is to obtain a careful history and knowledge of the exact details of the accident. Description of the tools, materials, and other objects used at the time of the injury is often valuable. Information about what the patient was doing and the direction and speed at which the missile entered the eye and whether or not there may have been more than one missile will help the ophthalmologist in the clinical management of the case.

Once the diagnosis of an intraocular foreign body has been made, its probable structure or alloy composition and its magnetic properties must next be determined. If a foreign body is nonmagnetic, it is important to know whether it is chemically active or inactive. Chemically active foreign bodies should be removed as soon after the injury as possible. Bodies of this kind include copper and its alloys, brass, lead, mercury, and the high manganese steel alloys. Wood is an irritant and should be removed. Chemically inactive foreign bodies include glass, coal, pure aluminum, gold, silver, platinum, and other inert metals. Plexiglas and other plastic materials also fall into this group. These substances may be let

alone unless the bodies are very large or unless they are pressing on vital ocular structures.

An accurate clinical examination of both eyes is the next step. This should include testing the visual acuity of both eyes with and without correction for distance and near vision and, if necessary, through a stenopaic aperture. The routine examination of the fellow eye may reveal evidence of an old healed perforation or even an old foreign body in that eye. The question of preexisting eye disease is also important. The examination should be made thoroughly with the use of a binocular loupe and focal illumination. The pupils should be dilated and an ophthalmoscopic examination should be made with special attention to possible hemorrhage or vitreous opacities. Steel may sometimes be seen as a silvery or black object in the fundus. Copper or brass often transmits a golden sheen. A yellowish exudate in the vitreous may simulate copper or brass. Air bubbles in the vitreous may also occasionally simulate foreign bodies. Slit lamp examination should be used routinely, and transillumination may reveal tears in the iris, hemorrhages, and the like. Measurements of the intraocular pressure may reveal a soft eye indicative of a perforation. Other auxiliary studies should be made as indicated. Even when the clinical examination fails to reveal an abnormality, each eye in which injury is suspected should be examined by roentgenogram. If a foreign body is found, it must be localized with extreme accuracy because the success of the operation and the site of the incision depend on exact localization. Several methods of roentgenographic localization are available, but perhaps the most useful tool for the diagnosis and accurate localization of magnetic intraocular foreign bodies is the Berman locator, which was first tried in December 1941 and which has since been accepted enthusiastically by military and industrial ophthalmologists. This instrument is even of some value in cases involving nonmagnetic foreign bodies, if they contain more than 12 per cent manganese.

Next in importance to accurate localization is the time of removal. The best time for the removal of a foreign body is before it becomes encapsulated. In fibrin, this occurs in 24 hours; in exudate, within the next 24 to 96 hours; and in connective tissue within from 7 to 10 days. If possible, the removal should be attempted within 24 hours after injury. If several nonmagnetic foreign bodies are present, however, no attempt should be made to remove them because such attempts always fail.

Before proceeding with actual surgical operation, it is well to assess the extent of damage to the eyeball. Although it may be necessary to enucleate certain eyes, this procedure should be postponed unless the injury is extensive. Twelve days has been accepted as the absolute limit of safety for sympathetic ophthalmia, but severely mutilated or hopelessly damaged globes should be removed before this arbitrary deadline if sympathetic ophthalmia appears likely. Nevertheless, it must be remembered that preservation of useful vision or of the eyeball is possible perhaps for the entire lifetime of the patient in spite of the retention of a foreign body in the posterior segment of the globe.

The actual technique for removal of a foreign body depends on its location

and magnetic properties. If the foreign body is in the lens and is not causing any irritation, it is best not to disturb it. If the lens is opaque, the foreign body and the lens should both be removed by the extracapsular route if the patient is less than 30 years old and by the intracapsular route if he is more than 30 years old. Either the anterior or the posterior approach may be used for the removal of magnetic foreign bodies in the posterior segment. The anterior route is easier and safer, and is generally used when the foreign body can be drawn forward into the anterior chamber around the edge of the lens through the pupil. It can then be extracted through a corneal incision, or if necessary by means of a posterior sclerotomy.

In extracting magnetic foreign bodies, it must be remembered that the hand magnet is a contact instrument and that unless the foreign body can be approximated within at least 2 mm., it is useless to try it. The giant magnet, on the other hand, has a wide magnetic field and permits the dislodgment of an incarcerated particle. Retinal detachment is avoided when the posterior approach is used, but the procedure may be complicated by hemorrhage. This approach is especially indicated in cases in which the foreign body can be removed through a posteriorly placed wound of entrance, those in which the foreign body is too large or so shaped that it is inadvisable to carry it through the suspensory ligament, and those in which it seems to be entangled in the retina or the choroid, or both.

Foreign bodies in the vitreous when the lens is clear can sometimes be removed under ophthalmoscopic observation with a small forceps thrust through a meridional scleral incision. The choroid is incised with a cutting diathermy current. The scleral wound must be closed with sutures. In surgery involving the vitreous, care must be taken to avoid anything that will lacerate it further, such as blind groping. The ophthalmoscopic endoscope, designed for the extraction of nonmagnetic foreign bodies lodged in the posterior segment, should be used before infiltration and condensation of the vitreous have had time to occur. Otherwise it may be impossible even to grasp the foreign body within the endoscopic forceps. Transillumination may prove useful in cases in which the media are opaque. Corneal and scleral lacerations heal better and earlier when sutured. Hospitalization and absolute bed rest are essential, and atropine is used routinely after operation unless contraindicated by preexisting glaucoma. The patient should be kept under observation for a year or longer after a penetrating eye injury so that any evidence of sympathetic ophthalmia can be detected at once. Both eyes should be given a careful slit lamp examination and ophthalmoscopic examination at regular, frequent intervals.

SOME REFLECTIONS ON THE SUBJECT OF PENETRATING WOUNDS OF THE EYEBALL

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Immediate closure of the injured globe is the most imperative need confronting a surgeon called on to treat penetrating wounds of the eyeball. The advent of antibiotics has undoubtedly improved the vital prognosis of eyes so injured, but little as yet been accomplished in the way of improving the functional outcome. It should be possible, however, under cover of antibiotics to work out a method of treatment that would be based on the use of the conserved tissues. First, it must be remembered that the eyeball is a sphere composed of various tissues, some transparent and some opaque, the reciprocal anatomic positions of which should be respected. A penetrating wound, however, creates a focus of infection, brings into contact tissues that are normally separate, disturbs their orderly arrangement, and, most of all, leads to the formation of cicatricial adhesions and the opacification of the transparent tissues. Treatment, then, should be designed to overcome infection and relieve contusion, reestablish the anatomy of the globe, and prevent opacification. Better results will not be obtained until the surgical rules for the treatment of wounds in general can be applied to wounds in the globe. The most important of these rules—dressing and excision of the wounds and the immediate replacement of the excised tissues with grafts of the same kind—cannot be put into practice unless suitable grafts are available at the time of operation. This, in the case of corneal grafts, is virtually impossible but experimentation should be directed toward overcoming the difficulties insofar as possible.

One cause of reduced visual acuity after a penetrating wound that is often overlooked is the severity of the chorioretinal lesions accompanying the shock. Visual function is often compromised at the outset by the simple phenomena of contusion and chorioretinal concussion. Percussion, caused by a small, swiftly moving projectile, and contusion, caused by one that is larger and moves less rapidly, differ greatly in their dynamic effects. Lesions due to impact are often masked by the opacity of the tissues or else are so small that they are not visible on ophthalmoscopy, and there is a tendency to attribute the immediate loss of function they entail to opacification alone. The possibility of their existence' however, should always be taken into consideration as one of the factors affecting the outcome.

Each of the ocular tissues presents certain special problems, the clinical aspects of which are discussed in the light of the author's extensive experience with the wounded. First, the problem of infection dominates the whole subject of penetrating wounds, regardless of the site of penetration, varying only in intensity and

gravity according to the tissues affected. Antibiotics are, of course, helpful, but they do no more than retard the growth of bacteria, reducing it in time and in intensity. Sterilization of the wound, if it is obtained at all, is obtained at the price of cicatricial reaction, adhesions, opacification of the tissues, and trophic disturbances. The problem of inflammation, then, has both a medical and a surgical solution. The surgical solution is the one considered here.

Two points in connection with the nature of the foreign body deserve emphasis: (1) the severity of the lesions caused by splinters of wood or bamboo, and (2) the gravity of the threat to vision when the foreign body is made of copper—only when it could be successfully extracted was it possible to save the globe, and the degree of vision preserved depended on the speed with which the operation could be performed.

Lesions of the lens lead to its opacification, either immediately after the injury or some time later. A special problem arises in connection with the time at which operation can best be carried out. Matter in the anterior chamber and within the capsule should be aspirated at the time of the first operation, which must be performed as quickly as possible because of the external wound. Frequently, however, all the matter is not opacified or it has not become soft enough for easy extraction. Matter of this kind that has been left in place must be removed at a second operation. Again if the wound was caused by very small foreign bodies, mostly telluric in nature, the lesion in the lens may close spontaneously, leaving the foreign bodies in the lens parenchyma or in the anterior part of the vitreous. When telluric foreign bodies, which are extremely septic, are carried into the anterior vitreous, they lead to the formation of genuine lenticulovitreous abscesses. Treatment in each of these contigencies can be greatly simplified by using the method of artificial maturation by dilaceration of the lens matter with Sourdille's knife. This procedure should be carried out whenever there is reason to fear the formation of a lenticulovitreous abscess, or when the initial aspiration of the lens matter was incomplete. Since its adoption, lenticulovitreous abscesses have not presented any difficulty and the period of congestion in the globe has been decidedly shortened.

The corneal problem is inseparably connected with that presented by lesions of the iris. The author's experience shows that gelatin sponges can be used to keep a herniated or impacted iris in place after its reduction. Gelatin can also be used to separate the cornea from lens matter. Unless the operation can be carried out in aseptic surroundings, however, it is better to excise any herniated element. In two cases, a translucent fibrous formation developed in the anterior chamber, appearing first in connection with the iris lesion. In another case, in which an iridectomy had been performed, no such complication occurred. In this connection, the injury to the corneal epithelium must be considered in addition to the iris reaction. Large corneal wounds present all the conditions needed for fibrinous reaction and as a result extensive iridocorneal adhesions often appear. Only two solutions are possible, simple excision, or excision and immediate replacement with grafts of healthy tissue.

Wounds affecting the ciliary body have long seemed insoluble, but encouraging

results have been obtained in three cases by prudent excision of the affected tissues after extraction of the splinters, the use, in one eye, of a scleral graft, and the placing of a few perforating electrocoagulations around the wound to secure hemostasis. Small cicatricial areas are produced by the electrocoagulation, but they are aseptic, regular, and infinitely less dangerous than the large infected area of the lesion itself. The operations were perfectly tolerated and the postoperative course was remarkably tranquil.

Comment: The use of antibiotics and the corticosteriods has materially improved the prognosis in penetrating injuries of the eye. At the University of Chicago Clinics we administer 1 Gm. of chloramphenicol as early as possible and then administer 250 mg. every four hours until certain that purulent infection is not going to develop. Usually it may be discontinued within two or three days. Additionally, 80 U. of ACTH is administered daily in divided doses for four days, then reduced to 40 U. for two days, and to 20 U. for a final two day period. Although there has been no direct evidence to prove it, we believe that the routine administration of ACTH prevents the development of sensitivity to uveal pigment which may well predispose to sympathetic ophthalmia.

In recent years there has been a distinct tendency to suture wounds of the eye with intrascleral and intracorneal sutures using the Grieshaber or Ethicon needles. A surprising number of eyes are retained which in previous years would have been enucleated.

The author of this interesting paper points up two interesting points. Wood and vegetable fragments, since they travel so slowly, seldom are sterile when they enter the eye and for that reason are very likely to produce a purulent inflammation immediately. Such injuries are probably an indication for subconjunctival injection of an antibiotic. We do not believe this is necessary for metallic fragments which tend to sterilize themselves because of the heat created by their high velocity. Copper foreign bodies, which excite a typical reaction only when more than 85 per cent copper is present, cause a sterile purulent inflammation and, unless removed, may destroy the eye. This is not true, however, when copper lodges in the lens where it is remarkably well tolerated for long periods.

Generally, it is best not to remove lens material at the time the intraocular foreign body is removed unless the lens has been badly injured. In such injuries there is usually a mixture of lens capsule, cortex, and vitreous in the anterior chamber and everything one does in excess of what is absolutely required leads to further disorganization of the globe.

FRANK W. NEWELL

THE ORBIT

ETIOLOGY AND PATHOGENESIS OF PULSATING EXOPHTHALMOS

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The authors describe a case of pulsating exophthalmos in a 40 year old man who had sustained a gunshot injury. The point of entrance was in the area of the left zygomatic arch. The projectile advanced to the area of the second cervical vertebra from which it was later removed. It injured the third branch of the trigeminus, the vagus, and the hypoglossal nerves, and had perforated the internal carotid and vertebral arteries, branches of the external carotid artery, and the jugular vein. A large aneurysm developed into which the vertebral and occipital arteries opened, while the internal carotid artery was obliterated. The blood flow from the aneurysm was partly by way of the dilated cervical veins, but mainly by way of the peripheral stump of the jugular vein in the direction of the skull. A flow directly in the direction of the heart, which is a common occurrence with arteriovenous fistulas, was prevented by the occlusion of the central stump of the jugular vein. An angiogram showed that the external carotid artery of the injured side participated in collateral circulation by way of anastomoses with the internal carotid artery. Although the amount of blood which thus was carried to the brain may have been relatively small, it may still have been decisive with regard to compensation for the deficiencies of the internal carotid and vertebral arteries.

The occurrence of pulsating exophthalmos in the presence of an extracranial arteriovenous aneurysm is unusual. It demonstrates that the arterial pressure is continued to the orbital veins by way of the jugular vein, the transverse sinus, and the inferior and superior petrosal sinuses. Such an extensive reversal of the blood flow in the venous portion of an arteriovenous fistula can be explained only by the occlusion of the peripheral stump of the internal jugular vein.

The conclusions drawn are as follows: An arteriovenous aneurysm between the great vessels of the neck may cause a pulsating exophthalmos if, as a result of the occlusion of the jugular vein centrally from the aneurysm, the venous blood cannot flow directly toward the heart but is compelled to make a detour by way of the endocranial sinuses, the sinus cavernosus and the orbital veins. The effects on the cerebral circulation of this reversal of the blood flow in the venous circulation depends on the site of the aneurysm. A site close to the central portions of the common carotid artery and the jugular vein in unfavorable because formation of a collateral circulation by way of the orbital and facial veins is excluded and

the blood flow must take its course by way of the venous system of the opposite side through the transverse and intercavernous sinuses. Relatively more favorable are the conditions in those cases in which the arteriovenous short-cut with occlusion of the central venous stump is situated distal from the juncture of the facial vein because the usual flow of blood by way of the orbital and facial veins can develop without obstacle into the portion of the jugular vein which is situated centrally from the aneurysm. There is no need for special reference to the fact that the discussed conditions cannot be equaled with the simple occlusion of the internal jugular vein without formation of fistula.

Comment: In penetrating injuries about the orbit almost anything can happen in the way of abnormal arteriovenous communications, and usually does. The authors' interesting case bears out this statement. In the original text, they report that the retinal veins of both eyes were dilated, a certain indication of the tremendous enlargement of the veins of the head rostral to the area of aneurysm. This particular patient was fortunate in that the jugular vein "heart-ward" was occluded, otherwise there would probably have occurred a marked cardiac hypertrophy. This hypertrophy is often compared to the cardiac changes that result from aortic regurgitation.

For those who may be interested in another unusual arteriovenous communication in the neck with involvement of the jugular channels, the reader is referred to the report by Terry and Mysel (J. A. M. A., 1934, *103:* 1036).

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GENERAL OPHTHALMOLOGY

DERMO-OPHTHALMOLOGY

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Lancet, 1957, *1:* 1003–1006

Speaking of the field of dermatology some 70 years ago, Jonathan Hutchinson said that "beyond all others it offers attraction to the student of the laws of disease, and to the seeker after the causes which disturb health and local nutrition." He was quite right. Some branches of modern medicine have little obvious relationship with each other and only slender links with general health; but nobody can reasonably deny that the skin and the eyes may act as mirrors to each other and to the whole bodily state.

Bearing in mind the fact that certain differentiated elements in the eye are derived from the embryonic ectoderm, opthalmologists may naturally expect that some of the hereditary and environmental factors which help to determine the state of the skin will also influence the eye. This expectation is abundantly fulfilled, because there are in fact innumerable instances of parallelism in dermal and ocular pathology. Thus thyroid deficiency can bring cataract as well as alteration in the skin texture. Another disease notorious for attacking eyes and skin is Boeck's sarcoidosis. Fundus lesions may be associated with sebaceous adenoma of the face in epiloia. Facial nevus may supply the clue to retinal angiomatosis in Hippel-Landau syndrome. Von Recklinghausen's disease also manifests itself in the eyes as well as in the skin.

The eyelids, which normally serve as eyeshields, sometimes also act as a bridge by which infection and other noxious agents travel from the skin to the eyes. In addition, the lids themselves are a favorite site for basal cell carcinoma and may be implicated in and distorted by facial lupus. Xanthelasma, xeroderma pigmentosum, and psoriasis may also occur in the palbebral skin and produce consecutive changes in the eye. Nearly all the acute infectious fevers are characterized by a rash, and many of them also provoke ocular complications. Syphilis, in spite of its decreasing frequency, can still produce a wide range of skin and eye lesions, so that it occupies an important place in differential diagnosis.

As the skin of the eyelids is more sensitive than any other part of the integument, it is commonly the first to be affected by noxious physical and chemical influences, and it may also flare up as a result of dermatitis beginning elsewhere. Nutritional defects, too, including a lack of vitamins, may have their effect on the skin of the eyelids.

Mistakes in diagnosis and delay in arriving at a correct diagnosis could often

be prevented if the whole body surface were examined. Time, however, is fleeting and since ophthalmologists are seldom able to make a complete examination, they should always be on the alert for the information to be obtained from whatever skin is open to view. Clearly, the face is the most important, but the head and neck should not be neglected, and even the hands can supply valuable pointers, as in the case of a patient with failing vision whose fingers showed a brownish-yellow discoloration indicating tobacco amblyopia, a diagnosis later confirmed by detailed examination.

Dermatitis of the eyelids is perhaps the most important of all the subjects that jointly concern skin and eye specialists. Even if the origin of a patient's lid eczema is obscure at first, it will be easier to track it down if an effort is made to describe all the relevant signs in writing at the outset. The first of these signs is a change of color, which can be recognized from afar in all but the slightest degrees. Acute dermatitis of recent onset often produces a pink flush, but brownish discoloration suggests longstanding trouble. In chronic marginal blepharitis the lids may turn dark red. Next to be considered are the eyelashes, which may be altered in color or diminished in number. Crusts of dried secretions are sometimes entangled in the lashes, and the line of eyelash growth may be distorted. Finally, the skin surface may show fine additional wrinkles, branny desquamation, fluid droplets, adherent crusts, or even lichenification. There may be fissures, especially at the outer canthus or underneath a redundant fold.

Lid eczema, when it is not due to seborrhea, rosacea, or direct infection, is in most cases a reaction to some irritant substance, and the list of possible offenders lengthens every year. Anyone *may* react unfavorably to almost any substance. In addition to chemicals, cosmetics, and metals, dermatitis may be caused by various substances used for medicinal purposes, especially sulfonamide and penicillin. Dermatologists are apparently more aware than ophthalmologists of the disadvantages of topically applying these substances, as shown by the fact that when Borrie (1956) analyzed a large series of lid eczema patients, he found that cases of dermatitis medicamentosa formed the second largest group, and that two thirds of these originated from the prescription by ophthalmologists of drops and ointments containing these substances.

Although psychosomatic medicine is sometimes spoken of as though it were an entirely modern concept, the notion that bodily states may be produced or aggravated by stress of mind is as old as history. The fact that the skin mirrors the mental state in so many ways does not, however, mean that other factors, e. g. heredity, infection, and allergic susceptibility, should be ignored. Moreover, it should also be remembered that skin lesions are in themselves a source of worry. Sensitive people with a pride in their appearance and the habit of personal cleanliness are naturally distressed by rashes or blemishes on exposed areas of their skin, and the neurosis that sometimes ensues may be misinterpreted as the cause, instead of the effect, of the dermatitis.

Among the skin diseases that can create ocular havoc, few are more distressing than pemphigus and certain other vesicobullous conditions that lead to essential shrinkage of the conjunctiva. Not infrequently, pemphigus destroys the sight

of both eyes. Rosacea patients are particularly liable to meibomian cysts, mild blepharitis, and conjunctivitis. Anterior uveitis, side by side with skin lesions, may occur in syphilis, tuberculosis, herpes zoster, pemphigus foliaceus, and various other diseases, including sarcoidosis. Dermatogenous cataract, in which dermal and lenticular lesions are associated, is not well named, because the skin changes are clearly not the cause of the cataract. The cataract itself usually appears in the third decade of life, about 10 years after the dermatitis has begun. It is an interesting fact that the removal of a dermatogenous cataract is apt to be followed by postoperative complications, including retinal detachment.

Finally, fundus changes may be related to changes in the skin, not only in the phakomatoses, but also in many other conditions, such as tuberculosis, syphilis, diabetes, and sarcoidosis. A very interesting relationship is that of angioid retinal streaks associated with the skin nodules of pseudoxanthoma elasticum.

INSTRUMENTATION FOR BIOENGINEERING

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Science, 1957, *125:* 871–873

Bioengineering is the field of applied science which is concerned with the application of the physical science techniques to problems in medicine and biology. Bioengineering also applies to the general area of the extension of normal and abnormal limits of human physical capabilities.

INTRAOCULAR PRESSURE MEASUREMENT

Consider the problem of measuring the pressure inside the eye, which is of great importance in the detection of glaucoma. It is not practical to put a pressure probe inside the eye. Usually this intraocular pressure is measured by means of a tonometer, a special form of indentation-hardness tester that is placed over the eye, loaded with a given force, and indicates the depth of penetration. The reference plate rests on the rigid front of the eye and the moving plate on the cornea. Although it is a very useful instrument, the tonometer nonetheless has many drawbacks, and there is need for a better method of measuring intraocular pressure. We are working to develop such a method. A technique devised by Karl Sittel of our laboratories involves measurement of vibration of the eye. Nothing will touch the eye but a fluid column. Preliminary experiments indicate the feasibility of this method, and we are just starting a more ambitious program to develop and evaluate the technique fully.

READING DEVICE FOR THE PARTIALLY SIGHTED

Much work has been done in prosthetic and sensory aids to help handicapped individuals to perform normal actions in a more nearly normal manner. For instance, for the partially sighted we have developed the projection magnifier. This is an opaque projector which produces a magnified, high contrast image that can be read by a great number of the partially sighted who cannot comfortably read with other instruments. This device is an image magnifier, but many design problems of screen size, magnification, contrast, illumination, control of field of view for scanning, and material insertion had to be solved, in terms of the needs of the partially sighted, before the development was completed. A large scale research and test program was undertaken for the purpose.

The first projection magnifier that we made was a walk-in model which required 18 automobile head lamps of 32 candlepower each and, naturally, a large blower to keep the reader from being baked alive. In tests of this model with a number of subjects, relationships between visual acuity, reading speed, and magnification were determined. We came to the conclusion that for people who needed 10 times or more magnification, reading required considerable effort, and not many of them were sufficiently interested to take the trouble.

We also learned—and this seems obvious in retrospect—that persons with poor visual acuity tend to press their eyes close to the screen and move their heads as they read across the line. Even when manual control of scan was provided, many preferred to leave the material alone, scanning as much as possible by head rather than by hand motion. This was even more likely to be true as visual acuity decreased. Finally, we concealed all but a small portion of the screen and determined the reading speed and comprehension of children with the small screen as compared with the large. The differences were small, and the economic advantages of the small machine and the small screen far outweighed the minor improvement in performance with the large machine.

The small screen projection magnifier was then developed and subjected to preliminary test with partially sighted individuals of all ages. Thereafter, 50 test units were constructed and carefully evaluated in a two year test program. The results of the evaluation revealed a need for this type of device and pointed out the advantages and deficiencies of the test models. Since that time, a commercial producer has been licensed to manufacture and distribute projection magnifiers of an improved design, thus bringing the partially sighted a new reading aid. The same optical principles are being applied to an industrial inspection device. Thus, this work not only has benefited the class which we originally set out to help but is serving industry as well.

GUIDANCE DEVICES FOR THE BLIND

Several programs of development of devices for the blind are also currently under way. One phase of the problem, navigation, is being worked on in several places. Guidance devices based on more sophisticated principles than that of an ordinary cane have been undergoing development since World War II.

These devices are intended to permit a blind traveler to get about more safely, more rapidly, and with less stress than is possible with a guide dog or an ordinary cane. They employ ranging and proximity principles. They use ambient and self-generated radiations. They use sound, light, radio, and radar. While none have yet gone very far beyond the development laboratory, these instruments are good examples of bioengineering developments which involve adapting known engineering techniques to a new setting. At all the meetings of those working in this field the most significant discussions are likely to be about the requirements for such guidance devices, the characteristics of the people who are to use them, the situations in which each device is or is not suitable, and the many intangibles, rather than about engineering features. The basic philosophic design problems are much more difficult to answer than the engineering problems, and frequently it is very difficult to formulate the design problems in any satisfactory way.

READING DEVICES FOR THE BLIND

Other groups are striving to develop reading machines that will enable the sightless to comprehend ordinary printed material. These projects are not yet complete, but they are building an understanding of the requirements, and this is necessary before we can proceed with the proper development.

The crux of most bioengineering instrumentation problems is in setting the specifications; the development of reading machines for the blind illustrates this point.

The means for converting ordinary printed material into a code is well within the competence of those working in the field of commercial reading machines. Converting a letter-by-letter translation of the text into any other reasonable code is possible with modern computers. For instance, the converter could use the contractions used in advanced Braille. All this would be expensive, and whether it is worth while depends on how many of the blind read Braille or, more important, on how many would read Braille if there were a greater range of material available.

Or is the problem of reading one's own mail even more important? How many of the blind would go to how much trouble to learn to use a device that would let them read their own mail, labels, and so on? Just to read a cookbook might mean a great deal to someone.

SENSORY SUBSTITUTES

Fitting the physically handicapped to take useful places in industry is another field of great interest to the bioengineer. Our own experience has been limited to the problems of the blind, but we have developed sensory substitutes which enable blind workers to perform tasks that would not otherwise be possible. Substitutes may range from very complex devices to the very simple, such as a conducting brush and conducting plate used to find holes in a thin mica sheet. Much more of this kind of thing can and should be done.

Along these lines we expect to begin an extensive program of job engineering for the physically handicapped. Simple devices would be of the type that enables

a blind person to read a gauge. There are, for instance, many jobs that could be performed by a blind worker except for the fact that a dial must be read. Optical inductive, or capacitative sensing units could be developed, which the blind worker would apply to the dial face to convert the dial reading to an auditory or tactile signal. In other jobs it is necessary that some mark be made on a record slip, and a simple reading machine might enable the blind worker to locate the proper place to be marked with his number.

A tremendous range of physical science problems and techniques, from all the branches of engineering, are involved in bioengineering instrumentation. The examples I have cited typify the problems that arise, but the techniques we have used represent only an infinitesimal fraction of the resources that we must exploit. The main challenge to the bioengineer is that of defining the problem in terms of what is useful and economically justified. One must understand the possibilities of engineering development and the probability that an effort will reach any assignable goal within a given time. Only then is it possible to work out a practical solution to the instrumentation problem. It is very easy to become so absorbed in the engineering development that we lose sight of the final goal and the purpose of the development. It is also easy, in working out an experiment, to become obsessed with the need for a particular bit of data, or of too great a degree of precision, without considering that the cost of obtaining these data might not be justified by their value to the full development. Thus, the only principles that can be generally applied to the bioengineering problem are those which would apply to making any decision that leans heavily on judgment.

Comment: Great technical advances are made at the expense of increasing specialization. Greater specialization enforces greater restriction of knowledge to ever narrower fields of endeavor. This circle, if not vicious, unfortunately makes knowledge of technical advances outside of one's own field limited, so that investigators may not be aware of techniques or instrumentation which would make the solution of any given problem very much easier. It is refreshing to know that at the Franklin Institute Laboratories attempts are being made to cross the boundaries of specialties and to apply recent advances in one field to another and unrelated field. Results as reported have not been conspicuously successful, and yet the mere fact that such investigations are under way is encouraging. It is hoped that work will continue until more concrete results can be realized.

DANIEL SNYDACKER

HEREDITARY DISEASE

DEVELOPMENTAL ANOMALIES OF THE SKULL AFFECTING THE EYE

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A. M. A. Arch. Ophth., 1957, *57:* 593–610

Previous reports on congenital anomalies of the eye in patients with developmental anomalies of the skull, which are widely scattered in specialty journals, have usually been limited to certain aspects of the problem presented by these patients. It seemed, therefore, that practicing ophthalmologists would find it helpful to have a general review with a broader scope. Further impetus was given to the work by the fact that many patients with anomalies of this description were seen at the Iowa State University Clinic within a comparatively short time.

Congenital anomalies of the skull have been classified in various ways, many of which are inconsistent or confusing. In this review, the classification used by Nager and DeReynier in their monograph on congenital anomalies of the ear associated with developmental anomalies of the skull has been followed, with adaptations to fit the special problems confronting the ophthalmologist. Accordingly, section 1 deals with anomalies of the cranium or the so-called craniostenoses or dyscephalias, which may or may not be associated with malformations of the extremities. Section 2 is concerned with anomalies affecting the cranium and the facial skeleton—the craniofacial dysostoses of Crouzon, again with or without malformations of the extremities. Section 3 is devoted to anomalies affecting the facial skeleton alone, consisting chiefly of the mandibulofacial dysostosis of Franceschetti in its various forms. Section 4 discusses hypertelorism, and section 5 summarizes certain rare anomalies. Descriptions of one or more representative cases will be found in each section, but no attempt has been made to report on all the patients.

1. CRANIOSTENOSIS

Anomalies may appear in the shape of the skull when the disappearance of a suture line and fusion of the adjacent bones take place earlier than normal. These anomalies are not pathologic unless they are pronounced and unless they cause clinical symptoms. Two main types of physiologic variations are distinguished: the long head, with an early disappearance of the sagittal suture (dolichocephalus), and the short head, with an early closure of the coronary or the lambdoid suture (brachycephalus). In the true craniostenoses, the bones fuse

along one or more suture lines so early that a disproportion between the skull and the brain is created. In roentgenographic films the convolutional outlines will appear prominent, and clinical signs and symptoms will be present. The true craniostenoses consist of tower skull (turricephalus, oxycephaly), which is a hyperbrachycephalic form and is probably the commonest of all; akrocephaly, in which the anteroposterior diameter is also decreased; and scaphocephaly, a rarer form in which the length of the skull is excessive and its breadth is diminished. Craniostenosis may be asymmetric; when the premature fusion occurs in only one half of the skull, asymmetry will appear and the skull will be plagiocephalic.

The symptoms presented by patients with craniostenoses are, first, those of increased intracranial pressure; headache, dizziness, and vomiting. Symptoms of brain damage, such as mental retardation and epileptiform seizures, follow. If the optic nerves are affected, vision will decrease. The deformed skull is the most prominent clinical sign. Anomalies of the nasal cavity and the palate are frequent, and deviations of the nasal septum may also be present. Damage to the eyes, which is a common though not inevitable accompaniment of craniostenosis, may take the form of blindness produced by atrophy of the optic nerve, exophthalmos, exotropia, and a few rare complications. Early operation is indicated not only to prevent mental retardation but also to protect the optic nerves and save the patient from blindness.

An example of akrocephaly with syndactyly was seen in an eight month old infant referred to the clinic because of a corneal ulcer in the left eye (Fig. 1).

FIGURE 1. Profile of an eight month old infant with tower skull and exophthalmos. (Courtesy of BLODI, F. C.: A. M. A. Arch. Ophth., 1957, *57:* 593–610.)

There was bilateral exophthalmos, and the child was unable to close the lids on the left side. The skull showed a typical tower shape, and the four lateral digits were fused in all four extremities. A lid adhesion operation was performed on the left side and the corneal ulcer healed with a dense scar. Coronal craniectomy with orbital decompression was carried out on both sides.

2. CRANIOFACIAL DYSOSTOSIS

This combination of cranial and facial anomalies was first described by Crouzon, in Paris, in 1912. The skull is usually brachycephalic, with the markings of a fully developed turricephalus. The facial deformities include atrophy of the upper jaw with inferior prognathism and malocclusion of the teeth; a broad, hooked nose with frequent deviations of the nasal septum; a high palate; irregular implantation of the teeth in the upper jaw; and anomalies of the ear. Ocular changes are secondary to the orbital anomalies. The pupillary distance is characteristically widened (hypertelorism), and the shortened orbits lead to exophthalmos of varying degree. Exotropia is common, and the optic nerve may suffer from papilledema and atrophy as in other forms of craniostenosis. The anomaly, which is present at birth but becomes more conspicuous during the first year of life, is essentially hereditary, according to Crouzon, and a familial incidence is evident in many of the reported cases. If increased intracranial pressure is allowed to persist, it will cause headaches, convulsions, mental deterioration, and optic atrophy. Decompression operations are indicated, as in other forms of craniostenosis, and if they are performed while the increased intracranial pressure is still in an early stage, the results are promising.

An example of this condition was found in a four year old girl who showed some exophthalmos and a deformity of the face caused by aplasia of the maxilla (Fig. 2).

FIGURE 2. A four year old girl with aplasia of the maxilla. (Courtesy of BLODI, F. C.: A. M. A. Arch. Ophth., 1957, *57:* 593–610.)

FIGURE 3. A 12 year old boy with typical Franceschetti syndrome. (Courtesy of BLODI, F. C.: A. M. A. Arch. Ophth., 1957, *57:* 593–610.)

3. MANDIBULOFACIAL DYSOSTOSIS

The chief characteristics of this dysostosis, which is often referred to as the Franceschetti syndrome, are: hypoplasia of the facial bones, especially the malar bones and the mandible, creating the so-called bird's face typical of the patients with this syndrome; malformations of the eyelids; malformations of the ear; anomalies of hair growth; and other anomalies such as blind fistulas between mouth and ear and cleft palate. In addition to typical cases of this syndrome, incomplete, abortive, unilateral, and atypical forms have been reported. The condition is undoubtedly hereditary, and the developmental disturbances must occur early—during the seventh week of embryonic life. A typical case of this syndrome was presented by a 12 year old boy who was born with a marked malformation of the auricles (Fig. 3).

Changes around the eye in the classical form of the Franceschetti syndrome are confined to the anomalies of the lids and occasionally to an epibulbar dermolipoma and the combination of this syndrome with severe ocular anomalies appears to be rare. Nevertheless, two patients with this combination have been seen at the clinic. The patients were very intelligent but practically blind. The eyes were microphthalmic and congenital cataracts were present. One of these patients was first seen at the age of four months, and has since been seen at various intervals. Because of her vision, she attended a school for the blind where she made excellent progress. When she was seen at the age of eight years, her

FIGURE 4. An eight year old girl with mandibulofacial dysostosis. (Courtesy of BLODI, F. C.: A. M. A. Arch. Ophth., 1957, *57:* 593–610.)

physical development was certainly retarded and her expression was that of a wizened old woman (Fig. 4).

4. HYPERTELORISM

This term was coined by Greig to designate a wide separation of the orbits. The most conspicuous ocular complication is exotropia, which may reach enormous degrees. On the other hand, if the external rectus muscle becomes paretic, esotropia will result. Optic atrophy, microphthalmos, and microcornea have also been described. Patients with both craniostenosis and hypertelorism show that these two anomalies may be more closely associated than was originally assumed. The frequency with which hypertelorism is associated with malformations of various kinds makes it perhaps doubtful whether it is an independent anomaly at all. However, a few instances of isolated hereditary hypertelorism have been reported.

5. RARE ANOMALIES

Rare anomalies include such defects as premature fusion of paired parts, e.g., the orbits; congenital bony defects; and distant lesions with an indirect effect on the eyes, e.g., platybasia, which may decrease the volume of the posterior fossa and press on the brain stem and cerebellum, causing vertical or horizontal nystagmus.

Comment: Dr. Frederick Blodi's point, that a comprehensive review of the developmental anomalies of the skull and their pathologic ocular associations is needed, is well taken and timely. We are grateful to him for his classification, summary and discussion.

The association between such skull and facial skeletal anomalies and the accompanying ocular aberrations is not difficult to recognize when the entities are present in their full expression. What is important, however, is the ability to detect the relationship when only very mild skull anomalies or *formes frustes* are encountered. Urets-Zavalia ("Peristomodeal malformations," A. M. A. Arch. Ophth., 1956, *55:* 526–545) has capably emphasized this fact and has stressed that in strabismus with vertical imbalance mild malformation of the upper facial skeleton may be found consistently. This author, furthermore, has called attention to the important association of the "A" and "V" syndromes (vertical muscle aberration) with such anomalies of the upper facial skeleton.

It is of paramount importance that the craniostenoses be referred by the ophthalmologist to the neurosurgeon as early as possible (during first year of life) owing to the poor prognosis in untreated cases for vision, mental development and even for life. In the proper cases neurosurgical interference may assure a useful citizen instead of a tax liability. In Crouzon's disease and Apert's syndrome a dominant mode of inheritance may be encountered and genetic advice can be given by the physician to such families.

Mandibulofacial dysostosis is also a gene determined disease and exhibits a rather marked range of expressivity. Nevertheless I believe I must differ with Dr. Blodi's inclusion of his 37 year old female case as representative of this entity. The woman's alopecia, microcorneae, congenital cataracts (membranous), and so forth, are features more pathognomic of Hallerman-Streiff syndrome. The latter disease, so far as I have been able to gather from the literature, has occurred only sporadically and its inheritance pattern, if one exists, is as yet unknown.

Other developmental anomalies of the skull and/or skeletal system having ocular association include:

(1) Dysostosis multiplex.
(2) Osteopetrosis.
(3) Pyle's disease (familial metaphyseal dysplasia).
(4) Albright's syndrome (polyostotic fibrous dysplasia).
(5) Mucocutaneous syndromes.
(6) Bone marrow hyperplasia associated with erythroblastic anemia, sickle cell anemia, and chronic hemolytic icterus may occasionally be a cause of asymmetrical hyperostosis of the skull.
(7) Pachydermoperiostitis.
(8) Cleidocranial dysostosis (rare ocular change).

HAROLD F. FALLS

THERAPEUTICS

THE TREATMENT OF SJÖGREN'S KERATOCONJUNCTIVITIS

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Ophthalmologica, 1957, *133:* 255–259

The uncertainty that still surrounds the cause of keratoconjunctivitis sicca explains the many methods proposed for its treatment and the inconstancy of the results obtained by their use. Franceschetti, as early as 1942, suggested the possibility that disturbances of cellular respiration might be partly responsible for the syndrome and adovcated the use of vitamins of the B group, especially vitamin B_2. The biochemical studies of Vannotti and his co-workers, showing that patients with Sjögren's syndrome present disturbances of intermediate carbohydrate metabolism that are related to a lack of cocarboxylase, induced the author to supplement the Franceschetti treatment, which was and still is valuable, by the administration of cocarboxylase. Cocarboxylase is an enzyme that is required for the degradation of pyruvic acid, an intermediate product of the combustion of carbohydrates and occasionally of fats and proteins. Cocarboxylase is formed from vitamin B_1 by phosphorylation in the interior of the cells. Thus, in Sjogren's syndrome, the avitaminosis is not exogenous, but there is a poor utilization of aneurin for the synthesis of the enzymes of which it is a part. Cocarboxylase is available commercially in ampules of 50 mg. under the name of Berolase (Roche) or Bivitasi (Calosi). It is given intravenously, or possibly subcutaneously, daily, every other day, or at least twice a week. A course of 12 injections is usually sufficient, but the treatment can be repeated, if necessary, at the end of three months. In treating the patients in this series, the author supplemented the ampule of cocarboxylase with an ampule of B vitamin complex, because, even if a patient cannot synthesize a sufficient amount of cocarboxylase with a normal diet, he can synthesize more when he is given a massive supply of B complex vitamins, especially if cocarboxylase is also added. It is this need for massive supplies of vitamin B complex that gives the Franceschetti method its value; the author merely advises combining it with cocarboxylase.

The patients in this series were five women, aged 19 to 62 years, all of whom had reduced speed of lacrimation as shown by the Schirmer test. All complained of dryness of the mouth, and one had had rheumatic disease. Administration of the combined treatment was followed in each case by improvement of the ocular condition. This was especially gratifying inasmuch as three of the patients had previously been given other forms of treatment without success. The good results were often transitory, however, so that the treatment had to be repeated after a

certain time. An eyewash was prescribed in each case. Ointments were not well tolerated and the local use of cortisone was not only ineffective but often irritating. The fact that Sjögren's syndrome affects women almost exclusively seems to prove that endocrine factors play an important part in producing the condition. One of the patients was given a compound of testosterone and estradiol (Femandren, Ciba, three linguets a day) during the interval between two courses of cocarboxylase with good effect.

The author's results and those of others who have had similar successes seem to support the theory that Sjögren's syndrome is due to a lack of cocarboxylase. Further trials of this vitamin B-cocarboxylase method of treatment, especially in patients with severe forms of the syndrome, should prove interesting.

Comment: Many drugs have been recommended for the control of keratoconjunctivitis sicca. These include the administration of tear substitutes such as:

(1) Gelatin 0.1 per cent in isotonic solution.

(2) Methylcellulose solution: 0.33 per cent methylcellulose (4,000 centipose) in either isotonic sodium chloride solution or equal parts of Sorenson's phosphate buffer solution (pH 6.8) and isotonic sodium chloride solution. The addition of benzalkonium chloride in a concentration of not greater than 1:50,000 is advisable but stronger surface tension lowering agents usually prove irritating in this condition.

(3) 50 per cent gamma globulin diluted in saline.

(4) Ringer's solution, i.e., sodium chloride (9 gr.), potassium chloride (0.42 gr.), calcium chloride (0.24 gr.), magnesium chloride (0.2 gr.), sodium bicarbonate (0.5 gr.), dextrose (0.5 gr.), water recently distilled to make 1,000 ml. This solution, however, should be made up each day and is therefore very rarely used. Usually one adds 0.7 per cent gelatin to this solution and 3 gr. of chloretol as a preservative. As the latter solution has to be made up fresh and offers no greater symptomatic relief than other more stable and easier to prepare vehicles, it has largely fallen into disuse.

As most of these cases occur in women in the menopausal age group, hormonal therapy has been advocated.

Finally the closure of the lacrimal puncta, as advocated by Beetham, is used when all other local and systemic measures have failed and usually proves quite helpful.

Although the gross clinical effects of severe vitamin deficiencies are well known today, marginal or subclinical deficiencies require considerable elucidation. There should be better understanding of the earliest manifestations of a deficiency state if recognition and proper management are to be obtained. There is much to be learned of the importance of intermediary metabolism and the role of vitamins in the metabolism in ocular function.

One of the major functions of the B vitamins is in the intermediary metabolism of amino acids by acting as coenzymes in systems responsible for the normal ultilization of amino acids. If the balanced interplay between vitamins and amino acids is changed, metabolic upsets may occur.

Dr. Cuendet and earlier Dr. Franceschetti suggested that a deficient absorption or utilization of the B vitamins might interfere with carbohydrate metabolism and so upset the metabolism of the lacrimal and conjunctival glands to produce keratoconjunctivitis sicca.

As Cuendet has noted, Franceschetti since 1942 has suggested that these patients might respond to large doses of vitamin B complex, particularly vitamin B_2. Cuendet believes that the addition of cocarboxylase might facilitate something which is lacking

in the intermediate carbohydrate metabolism in these individuals and therefore feels that they will benefit from such administration. He reports a number of patients who were improved subjectively. Unfortunately, a number of these individuals had Schirmer tests before and after therapy and there was no improvement in the wetting of the filter paper, although they were subjectively improved. An essential finding would, of course, be the failure of the cornea to stain after therapy in this fashion. Recently it has been shown by electrophoretic analysis of tears that there is an alteration of the tear pattern in patients with keratoconjunctivitis sicca. It would be helpful and confirmatory if the electrophoretic pattern of tears showed a tendency to return to normal after the therapy suggested by Cuendet. Improvement in other phases of the Sjögren's syndrome, such as the dryness in the mouth and arthritic signs, would also be supportive evidence of the value of this form of therapy. It is a much less convenient form of treatment in that it requires intravenous administration preferably and possibly subcutaneous administration daily or every other day or at least twice a week for six weeks, and the treatment may have to be repeated after various intervals of time as the symptoms warrant. Therefore, this type of therapy will not usually be employed unless other more convenient measures fail or unless it also brought about relief of symptoms in other parts of the body at the same time.

IRVING H. LEOPOLD

VISUAL MANIFESTATIONS OF DIGITALIS POISONING: TWO CASES OF TOXIC AMBLYOPIA

EMIL FRANDSEN

Acta med. scandinav., 957, *67:* 51–59

Because the dose of digitalis necessary to obtain a maximum therapeutic effect is often close to the minimum toxic dose, signs of overdosage are not uncommon. As a rule they are divided into three groups: (1) local, (2) cardiac, and (3) central.

Local signs include the rare cases of diarrhea, interpreted as intestinal irritation. Cardiac side effects manifest themselves particularly as bradycardia and extrasystoles of various types, usually in pairs (bigeminy).

Symptoms from the central nervous system are now considered to include nausea, anorexia, and vomiting, interpreted as reflexes elicited from the periphery (which may be the heart) to the vomiting center. The rare psychic disturbances—depression, impaired memory and power of concentration, possibly excitation increasing to confusion and delirium, coinciding at times with the maximum effect of digitalis—have been explained by Weiss as the consequences of sudden alterations in the cerebral circulation including the emission of edema fluid and possible chemical changes.

The group of central symptoms also includes visual disturbances. Most textbooks only mention flickering before the eyes and colored vision, especially

yellow and green vision, but it does not seem to be generally known that therapeutic doses may induce serious eye lesions, such as toxic damage of the optic nerve and paresis of the ocular muslces. Disturbances of color vision were observed as early as 1785 by Withering, who reported on 163 personally studied cases with heart disease. As a rule the earliest sign is flickering before the eyes and various forms of subjective visual sensations, such as flashes of light and bright spots of various colors in the visual field, at times in the form of a regular scintillating scotoma. In addition, the patients often have quite marked photophobia, the symptoms being accentuated in strong light. The color disturbances are very often in the form of yellow or green vision, more rarely blue vision. Objective examination of the eyes fails to reveal any abnormality. The chromatopsia and other visual disturbances metioned above are of little importance and invariably disappear within a few days after withdrawal of digitalis.

The author reports on two cases of toxic amblypoia. The first patient was a 67 year old woman with no history of eye trouble, who had been suffering from pernicious anemia for four years and heart disease with auricular flutter for five or six years. She developed signs of retrobulbar neuritis with deterioration of vision to 6/60 in direct connection with digitalization. The amblyopia was attributed to the anemia and treated with large doses of B_{12} and liver preparation without having any effect on the reduced vision. The anemia proved to be well compensated and there were no signs of myelopathy. The patient went on taking digitalis for five months, but after the drug was withdrawn the vision was improved to 6/24 and 6/18, after which it remained sationary.

The second patient was a 60 year old man with rheumatic heart disease as well as a history of hemiplegia and hemianopsia who developed clinical and electrocardiographic signs of digitalis poisoning. He had visual disturbances (hallucinations with red and green patterns) and massive annular scotomas. After digitalis was withdrawn the vision improved considerably.

In the first case the condition was complicated by the coexistence of pernicious anemia which was first thought to be the cause of the optic nerve lesion. The true etiology was not therefore recognized until five months had elapsed. Retrobulbar neuritis in pernicious anemia is well known though not common. Young saw only one case among 515 patients. The visual disturbance may be the initial sign of pernicious anemia, but as a rule it is a later phenomenon, occurring at the same time as other neurologic symptoms. The anemia was adequately compensated in the case reported. She had no signs of myelopathy on neurologic examination, and intensive treatment with B_{12} and liver preparations failed to affect the visual impairment. The vision did not improve until digitalis was withdrawn, so there does not seem to be any doubt that this was a case of digitalis amblyopia. The symptoms were noted as early as one week after digitalis was started, but in a fairly large dose. At the same time there were mild symptoms of intoxication (nausea), but not the usual visual phenomena of flickering and chromotopsia. The possibility remains that the anemia contributed to the induction of the retrobulbar neuritis by virtue of enhanced vulnerability of the optic nerve. In this connection it is worth mentioning that Brown saw three patients with

chronic glaucoma who developed early and severe visual impairment on digitalis.

In the second case the condition was complicated by the sequelae of hemianopsia, but there does not seem to be any doubt about the diagnosis of digitalis amblyopia, as he also had other symptoms of severe digitalis poisoning and as the withdrawal of digitalis and the treatment given had a good effect upon the ophthalmic disorder.

Comment: There is no doubt that digitalis can produce ocular symptoms and signs. These were first recorded by Withering in 1785. The visual manifestations stressed by Dr. Frandsen are well recorded and documented in the literature. By adding cases in which the papillamacular bundle in the optic nerve appears to be involved by the use of digitalis, he stresses the importance of recognizing this possibility in the differential diagnosis of central scotomas. This type of disease process, namely that due to digitalis poisoning, is reversible if caught early and becomes permanent only if excessive doses of the drug are used or if medication is prolonged without realization of the proper cause. In most of the standard pharmacology texts one will find all of these symptoms listed, including diplopia, which the present article also stresses, as a possible complication of digitalis poisoning. Some of the visual effects due to digitalis may be of central origin.

Dr. Frandsen recommends the use of vitamin B complex and vasodilators in addition to cessation of digitalis therapy in the treatment of the papillamacular bundle lesions. He also considers the use of potassium as of potential value. Potassium has been recommended for the complications of digitalis administration for a number of years. The rationale for its use is based on the fact that potassium may be lost with edema fluid loss as many of these patients who receive digitalis also get diuretics such as Diamox or mercurial ones and this tends to lower the serum potassium. Many of these patients suffer from malnutrition and gastrointestinal disorders and are receiving steroid therapy, all of which would tend to aggravate this potassium depletion.

This article is of definite value for it calls to our attention the possibility of visual side effects of digitalis with which we are, of course, all familiar; but it is well to stimulate one's memory occasionally. In an excellent recent article (New England J. Med., 1957, there is a discussion of the therapeutic and toxic indices of digitalis. Although this paper stresses the cardiac toxicities, no mention is made of the central or ocular effects.

IRVING H. LEOPOLD

Basic Sciences

BACTERIOLOGY

BACTERIOLOGY OF AQUEOUS FLUID OF THE EYE CONTRIBUTION TO ETIOLOGY OF UVEITIS

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Klin. Monatsbl. Augenh., 1957, *130:* 215–234

In bacteriologic studies of the aqueous fluid of the eye some technical, biologic and clinical problems have not yet been solved. Although the technique of puncture of the anterior chamber is simple, the small amount of aqueous humor thus obtained makes the detection of bacteria difficult. The bacteria may be free, agglutinated, phagocytosed by leukocytes, or already absorbed or phagocytosed at the surface of large endothelioid cells. Each of these four possibilities corresponds with a stage of invasion. Free bacteria may as a rule be found immediately after perforation or at the onset of an acute uveitis or of a recurrence. Culture is occasionally possible in this stage, which may last from several hours to several days.

The case of a 38 year old patient with severe iridocyclitis associated with generalized febrile influenza is described in which many free bacteria were detected in the aqueous fluid on the sixth day. Cultures were not made. Clinical recovery had occurred four weeks later. Several months later the patient had a recurrence of the acute iridocyclitis, but then it was too late to obtain a positive culture. The agglutinated bacteria could be seen in the microscope but the culture remained sterile and recovery from the acute attack occurred again within four weeks. The case of this patient is rare, since in most other cases of acute endogenous inflammation it is not possible to detect bacteria in the aqueous fluid with such ease.

Paracentesis of the anterior chamber, however, may be much more promising in cases of infections occurring after perforation of the globe. A case is described of septic hypopyon in a 44 year old workman in whom puncture was carried out 50 hours after a foreign body had entered the eye. Many free streptococci were visible in the hypopyon. Irrigation of the anterior chamber with penicillin was done and only a few phagocytosed cocci could be seen after a second puncture five hours later. The eye was already blind and was enucleated.

A third case is described in which the eye had been perforated by a piece of wood. Many free bacteria were seen in the aqueous fluid and others which were already phagocytosed by leukocytes. Culture yielded *Micrococcus catarrhalis.* An injection of 1,000 units of penicillin was made into the anterior chamber and

the cultures became negative two to four days later. The bacteria were agglutinated in fibrin on the fourth day and on the ninth day cocci were still detected in a large endothelial phagocyte.

In four additional cases staphylococci, *Cloatridium perfringens*, *Bacillus mesentericus*, and *Pseudomonas aeruginosa*, respectively, were found after a long search in the aqueous fluid. Not only eyes with accidental injuries, but also eyes with late infections associated with aphakia and Elliot's trephining could be saved with rapid bacteriologic therapy. Some of these eyes still retained satisfactory visual acuity.

These cases show the importance of repeated paracentesis of the anterior chamber in cases of exogenous infection. Cases similar to those described can be considered as "experimental infections" in human beings in which the different stages of inflammatory reaction may be studied by repeated punctures of the anterior chamber. Four cases of endogenous uveitis in two men and two women between the ages of 30 and 64 years are described in which the causative agent could be established by the bacteriologic examination of the aqueous fluid and in which the same different stages of inflammatory reaction could be found as in the described perforating wounds. Of about 70 known strains of microorganisms, viruses, protozoas and parasites which may cause intraocular infections, about 30 could be diagnosed with the aid of puncture of the anterior chamber. Staphylococci were grown most frequently on culture.

Immuno-allergic phenomena play an important part in the pathogenesis and development of uveitis. The presence of bacteria in the aqueous fluid, which has been established by puncture of the anterior chamber, does not change the validity of the previous statement, but rather indicates local formation of antigens. Statistical reports by other workers show positive results of cultures obtained from the aqueous fluid in only 4 per cent of cases examined with the aid of the present method. Of a recent series of 900 eyes from patients in whom puncture of the anterior chamber had been performed, phagocytosed microbes were detected in 1.5 to 22.5 per cent, depending on the disease aspect.

Comment: Recovery of bacteria upon culture of aqueous humor samples has been reported sufficiently often to leave no doubt that many species of organisms can survive and multiply in the anterior chamber. The present report mentions 24 positive cultures out of a series of 418 attempts following anterior chamber puncture. Of particular interest is the intimation that a bacterial agent was positively recovered from the aqueous of four cases of endogenous uveitis. Scrutiny of the original paper reveals, however, that in only two of these four cases was the organism recovered on culture.

Accepting the fact that bacteria can gain entrance into the anterior chamber from the blood stream and through perforations of the globe, and admitting the difficulties of culturing bacteria from small samples of aqueous, we must still place the burden of proof upon an author to demonstrate the significance of bacterial etiology in nongranulomatous uveitis. Diligent efforts by M. J. King, Sr., and others have led to the conclusion that such an etiology is rare or unimportant in cases of nongranulomatous uveitis in this country. The present report suffers from a lack of statistics tending to prove that the situation is different in Zurich. On the other hand, even a few confirmed isolations are noteworthy

in a field where presumptive diagnoses are the rule. A larger series of cases must be investigated by aqueous humor culture before a definitive answer to the question can be given.

HENRY F. ALLEN

BIOCHEMISTRY

RADIOACTIVE ISOTOPES IN OPHTHALMOLOGY

THE CHARLES H. MAY MEMORIAL LECTURE

EDWIN B. DUNPHY

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Bull. New York Acad. Med., 1957, *33:* 310–323

Although a thorough basic knowledge of atomic energy can be obtained only by work and study under the guidance of a nuclear physicist, there are certain fundamental principles that every clinician must have at his fingertips if he wishes to understand their application to clinical work. Modern nuclear physics teaches us that the atom itself has an internal structure which can be split into subatomic particles and, since this fact is responsible for the very existence of isotopes, a brief review of the subject seems desirable.

The atom consists of a nucleus surrounded by an outer shell of lesser density. The nucleus, which constitutes 99.98 per cent of the atom, is made of protons, carrying a positive electric charge, and neutrons, which carry no charge. In the stable atom, the positive charges of the protons are balanced by the negative charges of the electrons, which swirl around the nucleus in various orbits of the outer shell. The atomic number represents the total positive charge on the nucleus and, since each proton carries one positive charge, the atomic number is equivalent to the number of protons. The mass number, which approximates the atomic weight, represents the sum total of the protons and neutrons in the nucleus. Subtraction of the atomic number from the mass number gives us the number of neutrons.

Whereas the atomic number determines the chemical nature of the atom, the mass number identifies the structure of the nucleus. For example, when a neutron is added to the nucleus, it does not alter the charge but it does change the mass. Thus, there may be two or more substances each having the same atomic number but different mass numbers. Those with mass numbers that differ from the mass number of the stable substance are called "isotopes." For example, stable phosphorus is P^{31}. Its nucleus contains 15 protons and 16 neutrons. P^{32}, P^{29}, and P^{30} are isotopes of phosphorus. They all have the same number of protons and electrons,

they behave in essentially the same way chemically and biologically, but, because of a disproportion in the normal neutron-proton ratio, their nuclei become unstable and disintegration takes place with a release of energy and radiation.

In 1934, when it was found that various stable elements could be made artificially radioactive by bombarding them with certain particles, such as deuterons, neutrons, protons, alpha particles, and the like, a whole new field of medicine was opened up in respect to the investigation of physiologic processes and the diagnosis and treatment of various conditions.

Radioactive isotopes exhibit characteristic behavior patterns that must be understood if the isotopes are to be used intelligently. Thus it is essential to know the type of radiation emitted, the energy of the rays, and the physical and biologic half-life of the isotope itself. Familiarity with the proper dosage and the nature of the radiation hazards, not only to the patient but to the handling personnel as well, is also indispensable. Most isotopes emit either beta or gamma rays, or both; only a few emit alpha rays. Alpha rays, which are the nuclei of helium, have very weak penetrating power. Beta rays, which are high speed electrons, are more penetrating. Gamma rays, which are part of the electromagnetic spectrum, are so penetrating that several centimeters of lead are necessary to block them. All these rays may give rise to ionization and photographic effects. The energy of the radiation depends upon the velocity and the mass of the particle ejected from the unstable atom. This is closely related to the degree of penetrability and ionization in tissue and can vary greatly with the particular isotope employed. For example, the beta rays coming from radioactive sulfur can be stopped by less than a millimeter of tissue and, hence, are difficult to detect *in vivo*. Beta rays arising from radioactive phosphorus (P^{32}) have a maximum range of 7 to 8 mm. and, thus, are very desirable for studying concentrations in the eyeball. Radioactive potassium (K^{42}), on the other hand, has penetrating beta rays of almost 20 mm., along with some gamma rays, and is therefore often useful for studying concentrations in deeper lesions in the body. The half-life of any isotope is the time period in which half of its atoms will have disintegrated. This will vary from less than a second in some of the artificially produced ones to a million years in some of the naturally occurring ones. From a practical point of view, the half-life must be long enough to permit the completion of the test but not too long because of undesirable total body radiation if it is to be injected intravenously. Fortunately, most isotopes are excreted rather rapidly, so that their biologic half-lives are shorter than their physical half-lives. Finally, for the detection of radioactivity, some sort of ionization chamber or Geiger-Muller counter will be needed. The Geiger-Muller tube is the most widely used type, particularly for counting beta radiations. Gamma radiations, however, are usually measured by a scintillation counter.

The uses to which radioactive substances may be put in the field of ophthalmology may be discussed under the general headings of (1) physiologic experiments, (2) diagnostic applications, and (3) therapeutic possibilities. Experimental studies in which radioactive tracers, especially radioactive sodium (Na^{24}), have been used to gain knowledge of the circulation of the aqueous have made it

possible to establish two important concepts which are generally accepted today and which have completely changed the ideas previously held about aqueous formation. These concepts are, first, that a secretory mechanism exists in the ciliary body and that ultrafiltration plays only a small part in aqueous formation, and, second, that the nonelectrolytes enter the anterior chamber by diffusion, whereas most of the electrolytes enter by secretion. Other important studies with isotopes have shown (1) that the regions of the ciliary body and optic nerve are the main portals of entry for sodium into the eye from the blood; (2) that the limbal plexus plays the predominant part in delivering tracers to the cornea (in rabbits), as compared with that played by the tears and the aqueous; and (3) that there is an increased permeability of the blood-aqueous barrier in the rabbit eye up to six weeks after irradiation with 2,000 r. Von Sallman and Locke, however, who demonstrated this increased permeability in 1951, do not believe that it plays an integral part in the pathogenesis of radiation cataract.

In the field of intraocular tumor detection, radioactive phosphorus (P^{32}) is still the isotope of choice because of certain well known advantages. By radio assay, it has been shown to concentrate more in the ciliary body, choroid, and retina, where most tumors are situated, than in the nonvascular tissues or intraocular fluids. Moreover, it is retained longer by malignant melanomas than by normal choroid, iris, or ciliary body. In spite of this usefulness in detecting malignant melanomas in the anterior and equatorial region of the eyeball, P^{32} has certain limitations which must be borne in mind to prevent erroneous interpretations. Its disadvantages arise chiefly in posterior lesions and are due not to any fault of the isotope but to a lack of adequate counters to be placed behind the eyeball.

The therapeutic applications of radioactive isotopes in ophthalmology have been limited by comparison with their use in other fields of medicine because of the danger of damaging delicate ocular structures. Various interesting attempts have been made to use isotope radiation, and some of these suggest hopeful possibilities for the future. So far, however, the most successful seem to be those in which beta applicators are used for superficial ocular lesions. Even in these caution is needed, because undesirable late effects are beginning to be seen.

Comment: In very lucid fashion Dr. Dunphy has summarized the present and potential value of radioactive isotopes in ocular physiology, diagnosis, and therapy. It is interesting to learn how much has already been done in ophthalmology with radioactive isotopes, and very stimulating to see how much remains to be accomplished.

This is an extremely timely subject, to which a great deal of attention is being paid now by the press as well as by the Government concerning the dangers of "fall-out" of radioactive energy from bomb explosions and the dangers from the use of radioactive materials for industry and research.

At the present time acute radiation injury usually occurs from accidental exposure to high energy accelerators, radioactive materials, or nuclear fission reactors. Injury and occasionally death result from disturbance at the cell level, and the eye shares in the damage produced by the acute radiation. The eye also shares in the chronic effects of repeated exposures to radioactive substances.

Research must continue in an effort to discover chemical agents which will protect against the untoward effects of ionizing radiation so that from the ophthalmologic point

of view the lens as well as other ocular structures will not be damaged. Some degree of protection is afforded by sulfhydryl compounds and from anoxia, but more successful compounds and ones with greater protective features should be uncovered.

Radioactive isotopes have been used for measuring the volume of fluid compartments of the body and for the studies of circulatory status in other areas of the body. Only recently Bettman and Fellows have tagged red blood cells with radioactive phosphorus and used this as a method of studying factors which may be altering ocular blood volume. This method has proved a great tool in the study of the experimental animal, but no satisfactory method with or without radioactive isotopes has been devised for study in the human eye. Dr. Dunphy has stressed the fact that P^{32} has proved of definite aid to our clinical judgment in the detection of intraocular tumors provided certain limitations are recognized. This test has several variables, and continued study with P^{32} or with other radioactive substaces may bring forth a more reliable method not only for anterior segment lesions but for posterior segment ones as well.

Although it is known that the cytotoxic action of radioactive isotopes rests on their ability to ionize molecules, there are countless sorts of molecules in each cell, any one of which could be ionized by radiations. Each molecule in a cell can react with another and this in turn with others, the combinations of interaction are vast. Much has to be learned concerning the effects of ionizing radiations on ocular tissues although considerable work has already been done by investigators such as Cogan, Von Sallman, Benedict, and others.

Dr. Dunphy mentioned many of the possible therapeutic uses of these substances. The therapeutic value depends largely upon localizing the action. Localization of the ionizing action of radioactive isotopes depends essentially on the biologic characteristics of a radioactive compound which will determine its distribution in the body. After the substance has been localized in the tissue, its effect on the tissue will depend on the type of irradiation which it emits. It is not inconceivable that substances will be found which can be made into radioactive isotopes that will have a preference for undesirable tissues in ocular structures. These may in this way be destroyed. Up to the present moment, only a few of the large number of available radioactive isotopes have had any trial in ophthalmology.

Physiologic aspects of radioactive isotopes have by no means been exhausted although considerable experiments have been performed. Several papers using radioactive isotopes in ophthalmology were presented at the Research Association meeting in June 1957. Dr. Smeltzer and co-workers discussed the distribution of radioactive sulfate in the developing eye, and Wortman and Strominger used radioactive sulfur to study the mucopolysaccharides of the cornea. O'Rourke, Patton, and Bradley studied the uptake of radioactive phosphorus, zinc, and iodine by experimental malignant melanomas; and Freedman, Newell, LeRoy, and Okita investigated the tritium state in the rabbit eye. So we see that ophthalmic research workers are aware of the importance of this field and the wealth of information to be obtained from research along these lines. There is no doubt that much more work will be done with these agents from the diagnostic, physiologic, and therapeutic standpoints in the future.

IRVING H. LEOPOLD

Comment: Dr. Dunphy gives an excellent summary of the three major uses of radioisotopes in ophthalmology and in medicine generally. These are investigative, diagnostic, and therapeutic, and he points out the enormous benefits that have been derived from the employment of radiosotopes in these three fields. However, there is a negative side to the picture that bears mention. In a recent article Dr. Albert Schweitzer (The Saturday

Review, 1957), called for a halt of all testing of radioactive bombs. He pointed out that the end result of the indiscriminate addition of radioactive materials to the atmosphere was unknown but that evidence seemed to indicate that an increased incidence of leukemia and of genetic disorders was probable. In the same issue Dr. Libby of the Atomic Energy Commission (AEC) wrote a rebuttal to this plea and stated that the increase in general radiation due to bomb testing was infinitesimal. Recently E. B. Lewis (Science, 1957, *125;* 965) pointed out that there is a correlation between level of radiation and the occurrence of leukemia in the general population. He concludes that any amount of added radiation increases the incidence of leukemia.

Since the present world situation apparently makes a certain amount of atom bomb investigation essential, it behooves the clinician to keep all other radiation to a minimum. This brings us back to Dr. Dunphy's article and the general comment that although the use of radioactive isotopes for diagnosis and therapy is valuable, it should be used only when the usual clinical measures have been exhausted and not as a substitute for them.

DAVID SHOCH

THE KAYSER-FLEISCHER RING: A HISTOCHEMICAL AND ELECTRON MICROSCOPE STUDY

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Neurology, 1957, *7:* 341–355

Although the Kayser-Fleischer ring has come to be recognized as characteristic of hepatolenticular degeneration, its unique appearance and significance are still the subject of much study, speculation, and controversy. Ever since Kayser first noticed the peculiar coloration at the limbus of the cornea, and its association with cirrhosis of the liver and pseudosclerosis was described by Fleischer, attention has been focused on this phenomenon as representing a generalized metabolic disturbance having a common origin with the diffuse glial changes in the brain and cirrhosis of the liver. It was this aspect of the problem that prompted many investigations dealing with the Kayser-Fleischer ring, because it was justifiably assumed that elucidation of the composition of the ring would constitute a valuable clue to the identity of the metabolic or toxic process postulated by Wilson himself as probably responsible for the disease.

Early investigators, however, had two main obstacles to overcome. One was a lack of corneas for study and the other was the fact that in cases in which the cornea was removed after death, the Kayser-Fleischer ring was lost either in alcohol fixation or during the ether-ethanol treatment in celloidin embedding.

Furthermore, compositional differences found between corneas containing Kayser-Fleischer rings and normal human corneas could be related to the presence of a Kayser-Fleischer ring only by inference, because the microanalytic data referred to the cornea as a whole and not specifically to the corneal ring itself. These difficulties were responsible, in part at least, for the conflicting views that have been expressed about the chemical nature of the Kayser-Fleischer ring.

That the corneal coloration might be due to the deposition of some heavy metal was one of the earliest ideas entertained, especially in view of the resemblance of the corneal ring in hepatolenticular degeneration to the more superficial conjunctivocorneal ring of argyrosis. Another trend of opinion considered the corneal pigment to be derived from the breakdown of hemoglobin and the deposition of some polypyrrole derivative in Descemet's membrane. Aside from the frequently noted greenish tinge of the corneal ring, however, there seems to be no evidence to indicate any relationship to bile pigments and their derivatives.

Although the data obtained by Policard and co-workers, supplemented by the work of Brand and Takàts, proved that the cornea contains increased amounts of copper in hepatolenticular degeneration, the question of the relationship of the copper to the Kayser-Fleischer ring remained unanswered. The present investigation deals with the application of a modified rubeanic acid procedure for the detection of copper in situ. Corneas from two patients with hepatolenticular degeneration were studied. In the first case, since the Kayser-Fleischer ring was lost because of previous fixation with absolute ethanol, attention was focused on the deposition of copper in the substantia propria. In the second case the Kayser-Fleischer ring itself was studied and the presence of copper in the granules constituting the ring was demonstrated.

The histochemical and electron microscopic findings in the corneas studied showed that a clear distinction must be made in hepatolenticular degeneration between the accumulation of copper in the cornea as a whole and the highly specific morphologic changes in Descemet's membrane which consist partly of concentrations of copper in distinctive patterns in the Kayser-Fleischer ring. The accumulation of copper in the substantia propria appears to be a distinct phenomenon with a different origin from that of the Kayser-Fleischer ring. It should probably be considered a manifestation of the generalized increased affinity for the binding of ionic copper by tissues that characterizes the disease. Moreover, the specific distribution of this type of copper in the cornea argues for a specific binding property in the substantia propria. The copper detectable within the Kayser-Fleischer ring presents an entirely different problem. Here the copper was localized histochemically within fine granular deposits in Descemet's membrane. The deposits were arranged in two parallel zones of unequal width that were close to the endothelial surface of the membrane and were separated by a clear layer. Electron microscopy showed that the zones consisted of electron-dense inclusions arranged in the same pattern as the histochemically localized copper. Indications are that the copper in the Kayser-Fleischer ring is present in the form of a copper chelate and not in that of a copper salt. The color changes that have been observed in the ring are probably due to changes in its physical

properties (transmittancy, reflectance, and interference) rather than to the removal of some pigment.

Although the structural details revealed by electron microscopy and the other findings obtained in this study suggest the possibility that ionic copper loosely bound to albumin reaches Descemet's membrane by way of a diffusing substance, the reason why this copper reacts with some other normal or abnormal constituent of Descemet's membrane to produce the structural pattern of the Kayser-Fleischer ring is not yet known.

Comment: This paper makes several important points. It conclusively demonstrates that the heavy metal deposited in the cornea in so-called Wilson's disease is copper and not silver or any other substance. Secondly, the authors show that the copper is deposited throughout the substantia propria and not only in a ring near the limbus. What, then is the "Kayser-Fleischer ring"? It appears to be a deposition of copper in Descemet's membrane close to the endothelium. However, here the copper is not in the usual protein bound form but appears to be a chelate. (Chelation is the binding of an element, usually a heavy metal, by atoms from two or more molecules to form a ring structure. This is termed "sequestration" of the heavy metal. Familiar chelate compounds are hemoglobin and chlorophyll. A common industrial chelating agent is ethylene diamine tetraacetic acid, or EDTA. Grant has reported the use of this substance for binding calcium in the cornea.)

A word should be added on the role of copper in diseases of the central nervous system. The authors mention the deposition of copper in the liver and brain in hepatolenticular degeneration. Recently there have been a number of reports that indicate an abnormal elevation of ceruloplasmin in the blood of schizophrenics. (Ceruloplasmin is the copper binding protein of normal serum. The function of this copper protein substance is to oxidize certain amines such as *p*-phenylenediamine.) This seems to suggest that we are dealing with another "enzyme disease" such as galactosemia and sickle cell anemia. From this one cannot help but speculate that the solution not only of neurologic disorders such as hepatolenticular degeneration but also psychiatric disorders such as schizophrenia will be found in the further study of enzyme activity. Any old couches for sale?

DAVID SHOCH

RESEARCH ON THE VITREOUS BODY

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Modern Problems in Ophthalmology, Vol. 1, pp. 66–72, S. Karger, New York, 1957

Electrophoresis was performed on cattle vitreous which had been liquefied by high speed centrifugation and concentrated after discarding the sediment. This study permitted identification of four components: hyaluronic acid, serum albumin, and probably two globulins, one of which seems to be gamma globulin.

Measurement of the absorption of ultraviolet light in liquefied cattle vitreous revealed a maximum absorption band at 265 mμ between pH 5.0 and 10.0; this is predominantly due to ascorbic acid. The latter's concentration, calculated from absorption data, is 12 to 14 mg. per cent. Another absorption maximum observed in dialyzed vitreous gel at 277 mμ is caused by proteins. One author estimates that the central portion of the vitreous gel contains 3.2 to 3.3 mg. of tyrosine and 1.3 to 1.7 mg. of tryptophane per 100 ml. of gel. Using the whole vitreous body and applying a different method, another investigator found the same amount of tryptophane but three times less tyrosine. The albumin globulin ratio, estimated by spectrophotometry, is 0.46.

Vitreous gel liquefied by centrifugation and exposed to ultraviolet light showed a sharp drop in viscosity as a result of depolymerization of the hyaluronic acid.

The vitreous gel of cattle changes in composition depending on the age of the animal; in adult animals, there is a topographic variation in the composition of the gel. Hyaluronic acid content is very low in the vitreous of cattle embryos; it increases rapidly after birth, at the time when the greatest volume increase occurs in the vitreous body. The soluble protein is twice as concentrated in five-month old embryos as in adult animals. At birth it is only slightly above the adult level.

The calcium content decreases gradually from the fifth month until birth, when it reaches the adult level. At the third month of embryonic life the ascorbic acid content of the cattle vitreous body is almost that of embryonic blood. It reaches the adult level, which is 10 to 20 times that of adult blood, shortly before birth.

The total protein and the collagen content of the residual protein are highest in the ciliary region and lowest in the central portion of the vitreous body. Hyaluronic acid and the soluble protein are lowest in the ciliary region and highest in the cortical region.

Two groups of macromolecules are primarily responsible for the gel structure of the vitreous body. In adult mammals the gel appears to be constituted by a network of collagen filaments reinforced by large hydrated molecules of hyaluronic acid. So far it has been difficult to decide which is responsible for such gel properties as shrinkage, swelling, and rigidity.

Collagen is the main component of the residual protein, a term used to designate the structures which are removed from the vitreous gel by filtration or high speed centrifugation. The residual protein forms all the structural elements visible either with the light microscope or with the electron microscope in the vitreous body. According to one investigator, the residual protein consists of at least three components: collagen type proteins which vary between 50 and 90 per cent in different parts of the vitreous body; hyaluronic acid, contributing from 5 to 15 per cent; and noncollagenous proteins. An important component of the residual protein is vitrosin which belongs to the collagen class.

Some investigators have found that trypsin digested the hyaloid membrane and the coarse branching fibers of the ciliary region, but did not affect the fine filaments of the gel. The latter were digested by collagenase, but this enzyme did not digest the hyaloid membrane and the coarse fibers.

Hyaluronic acid is a polyelectrolyte formed by an unbranched polysaccharide. Its molecular weight, as determined by study of light scattering in hyaluronic acid prepared from vitreous gel, was found to be 300,000 to 500,000 with marked polydispersity of the molecules. By other methods the molecular weight was found to be 100,000 or even less. Discrepancies in molecular weights determined by these same methods have similarly been observed on deoxypentose nucleic acid. The length of the hyaluronic acid molecule in the vitreous gel was estimated by streaming double refraction measurements. One group found it varied between 1,000 and 4,800 A; another group found it varied between 7,000 and 10,000 A. The method of preparation was different in the two cases. The shape of the molecule has been described as a rotational ellipsoid and a randomly kinked coil.

Comment: The average ophthalmologist knows that the vitreous is a treacherous, slippery, unpleasant substance and he bends his efforts toward avoiding it completely rather than studying it further. If perchance he should become interested in this tissue he finds that a more intimate acquaintanceship only reinforces his original prejudice. It will not pour out of a test tube like a decent liquid, nor will it cut or lie on a spatula like a self-respecting solid. When he finally removes all the water he is left with a miserable, stringy, shred of protein about the size and weight of a wisp of cotton. Yet this little wisp has bound several thousand times its weight in water and is primarily responsible for the turgor and rigidity of the eye.

In an effort to understand how this minute amount of protein performs its vital function experimenters have stretched it, dissolved it, boiled it and subjected it to the scrutiny of various enormously complicated optical and mechanical devices. The results of these investigations are summarized here by Dr. Schepens. He has felt for a long time that derangements of the vitreous are primarily responsible for separations and tears of the retina (this thesis is nicely illustrated by H. Goldmann in his monograph, *Two Lectures on Biomicroscopy of the Eye*), and on this basis has proposed adjusting the volume of the globe to the volume of the shrunken vitreous. This mountain to Mohammed approach has been reversed by Dr. Shafer of New York who at the last Academy meeting reported successfully adding fresh vitreous to globes whose own vitreous volume was inadequate. Both these men are to be commended for their vigorous attack of the problem but, as Dr. Schepens points out, true progress awaits further knowledge of the etiology and pathology of vitreous disease and this in turn is dependent on more intimate investigations of the normal vitreous. And so back to the wisp of cotton.

DAVID SHOCH

COLOR VISION

DIAGNOSTIC TESTS FOR COLOR VISION

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Our equipment consists of a fairly elaborate lens and prism system by means of which two spectrums are formed. From one spectrum three radiations, usually a red, green and blue, are selected and combined in proportions which can be adjusted by the observer until the mixture matches the test color selected from the second spectrum. In addition to color matching, the apparatus can be used to determine the spectral sensitivity of the eye by measuring the relative brightness of different parts of the spectrum. A further type of observation is that of color discrimination in which the two halves of the field of view of the instrument are illuminated by beams of the same wavelength taken from the two spectrums; one of the wavelengths is then changed by a small amount until the observer can just detect a color difference. The magnitude of the wavelength step is then a measure of the discriminating ability of the observer at that wavelength.

Color vision testing forms an essential part of the medical examination of applicants to work on the railways, at sea, in the air, and indeed in a variety of other occupations where good color vision is required. Diagnosis for such purposes is generally limited to the question of whether the subject has normal or defective color vision.

MONOCHROMATS, DICHROMATS, AND TRICHROMATS

Three broad groups occur depending on whether one, two or three controls are required in color matching, and these are shown in an ascending scale of color discriminating ability. The "one-control" group, the monochromats, have no color discrimination and the visual image is made up of achromatic areas of varying degrees of lightness. The dichromats can do all their color matching by mixtures of only two radiations, selected according to the type of dichromat. The color discrimination of the dichromats is limited to certain parts of the spectrum only. Trichromats require three controls for color matching, and these are usually located in the red, green and blue parts of the spectrum. For normal trichromats, color discrimination extends throughout the spectrum, but anomalous trichromats exist with reduced discrimination intermediate between the normal trichromat and the dichromat. Their color matches, while still requiring three controls, differ significantly from normal color matches.

Color perception is mediated through the cone receptors in the retina, and the classification given above applies primarily to the rodfree foveal area of the

retina at high illumination levels. At very low illuminations, vision is mediated through the rods and all observers become monochromats. At intermediate illuminations and with extrafoveal vision, a somewhat subtle combination of rod and cone vision intervenes.

THE PROBLEM OF DIAGNOSIS

To diagnose abnormalities it would seem that we have only to establish, first, the capacity to discriminate colors and, second, the range of colors, if any, that are confused, in order to determine whether a subject has normal or defective vision and the type of defect. Yet the design of a simple test to give unequivocal answers to both these questions is no easy matter.

One of the difficulties is the absence of any standard condition of viewing under which a subject may carry out a test. In one test, small points of light are shown against a dark background, with the subject dark adapted. In another, the subject is light adapted, observes a card subtending several degrees and has to interpret a complex pattern of colored dots. In the Nagel anomaloscope, the subject peers through an eyepiece at a patch of light subtending less than a degree and is asked to adjust two knobs until the top and bottom halves of the patch, separated by a sharp dividing line, are identical in color and brightness. In yet another test, a series of colored disks mounted in black Bakelite holders have to be arranged in the correct hue sequence, the differences between one disk and the next being just detectable to a normal observer in a good light.

It is evident that several types of judgment are involved in these tests, and visual acuity, adaptation, light sensitivity, eye movements, contrast sensitivity, temperament, state of health, even the attitude of the examiner himself may influence the response of the subject. Added to this, differences of pigmentation, whether in the crystalline lens or the macular, may modify the quality of the light stimulus reaching the retina. Since these pigments are yellow in color, they tend to absorb the blue light in greater or less degree and thereby upset the reliability of tests which depend on discrimination between colors containing more or less blue.

TESTS IN CURRENT USE

(*1*) *Pseudoisochromatic Plates.* These plates, which perhaps we might describe more briefly and happily as confusion charts, consist of patterns of variously colored dots in which some figure or letter or other shape has to be recognized from its background. By the appropriate choice of colors, the charts can be designed so that they are read with varying degrees of success depending on the subject's color vision. The nature and number of the mistakes thus serve to indicate the type and degree of color vision defect. First, the reading of the charts is affected by the level and quality of the illumination, so that some degree of standardization is necessary for consistent diagnosis. Second, the complexities of color printing are so great that significant variations of color are liable to occur from one edition of a test to another. This is most unfortunate, since the evaluation of a test on the basis of extensive experience with it is liable to be invalidated

when a new edition is brought out. The only remedy to this seems to be to make even more stringent demands on the printer.

(*2*) *A. O.-H.R.R. Test* (*American Optical Company*). This test is based on studies made by Hardy, Rand, and Rittler (1954). The background of all plates consists of a pattern of gray dots differing in size and lightness while the colored patterns are printed in hues which are confused with gray by the three types of color defective (protan, deutan, and tritan) and indeed of a theoretic fourth type, tetratan, whose existence is yet to be established. Further than this, by printing the patterns, triangles, circles, or crosses in increasingly saturated colors provision is made for a quantitative grading of the defect as either mild, medium, or strong.

An occasional borderline case may be misclassified by this test because of the provision of only four plates to separate the normals from the slightly red-green defectives, a limitation which arises directly from the decision to use gray backgrounds only. Nonetheless this is the most promising of any of the confusuon tests, particularly from the diagnostic point of view.

(*3*) *Farnsworth-Munsell 100-Hue and Dichotomous Tests* (*Munsell Color Co., Baltimore*). The 100-hue test (Farnsworth, 1943) comprises a selection of colored papers from the Munsell atlas chosen to have approximated the same saturation or depth of color and the same lightness (at least for normal vision). They embrace a complete circle of hues, with approximately equal steps in hue between one sample and the next. To achieve this an original selection of 100 hues was reduced to 85.

The colored papers are mounted in dull black Bakelite caps which expose a disk of color 0.5 inches in diameter. The disks are numbered on the back and divided into four series, each covering a quarter of the hue circle. The terminal colors in each series are left in position at each end of a wooden panel, and the remainder of the colors are mixed together. The subject then has the task of rearranging them in their correct hue sequence between the terminal colors. This has to be repeated for all four panels.

The test is thus a test of color discrimination and has the great merit of including all the hues. It is therefore eminently suitable for diagnosing the different types of defect, since the ordering errors will occur at different places round the hue circle, depending on whether the subject falls in the protan, deutan, or tritan class. The magnitude of the positional errors will, in addition, indicate the degree of the defect. If the subject has a generally low discriminating ability but is not otherwise color deficient, then the errors will tend to be distributed uniformly round the circle.

The one serious limitation of the test is that on account of the abnormal spectral sensitivity of the protanope and protanomalous observers, the colored papers will not all have the same (protanopic) lightness, the red and orange colors in particular appearing darker than they do to the normal. It can therefore happen that a keen protan observer may be able to use these lightness differences to arrange the samples correctly or nearly correctly, even though his defect may be quite marked.

(*4*) *Nagel Anomaloscope.* As already mentioned, this is a color matching instrument in which a monochromatic yellow light has to be matched by a mixture of monochromatic red and green. If too red a mixture is required, this is an indication of protanomaly, while too green a mixture indicates deuteranomaly. However, it can be said at once that with intelligent use a good deal more information than this can be extracted from the anomaloscope.

Thus, a match should be repeated several times to test whether the subject is a dichromat. If he were, a number of different settings would be equally valid as a match for him, so that a single observation could be quite misleading. If dichromasy is suspected, the subject should be asked to match the yellow against the red alone and against the green alone, Protanopia can then be distinguished from deuteranopia by the excess amount of red required by the protanope to secure a brightness match between the two halves of the field. In the case of an anomalous trichromat, repetition of the match has the further advantage that the spread in the settings will give an indication of the color discrimination of the subject. Nelson (1938) has shown that the extent of the departure from a normal match is not necessarily directly related to the loss of color discrimination, so that if both can be studied, a more complete idea of the degree of the defect is obtained. Other checks on the subject's vision can be secured by asking him to name the colors he sees in the anomaloscope and also by getting him to comment on the appearance to him of the match made by a normal subject.

Since the anomaloscope is a fairly expensive optical instrument, it can hardly be expected to find such widespread use as the confusion chart tests. Its main limitation in a general purpose test is that it gives no information about the tritan class of defect.

(*5*) *Lantern Test.* The primary purpose of the lantern test is to determine a candidate's ability to undertake a job involving the recognition of signal lights. For this purpose, small apertures are illuminated by one of a limited number of colors—generally red, amber, green and white—which the candidate has to name. The size and intensity of the lights correspond as nearly as possible to those encountered in practice.

From the practical point of view, the test is one of the most important in use, yet while it will generally establish the existence of a color defect, it is of little value for diagnosing the type of defect. This is inherent in any naming test, especially where the selection of colors is limited.

(*6*) *Colorimeters Using Spectral Stimuli.* These instruments have two important advantages for diagnosing color defects. On the one hand, the three functions of spectral sensitivity, wavelength discrimination and color matching can be tested independently. On the other hand, the use of spectral stimuli virtually eliminates the confusing influence of ocular or retinal pigmentation, since the quality of a spectral radiation is unchanged by passage through a pigment layer. A comprehensive examination with an instrument of this type may take several hours or days, although it is frequently possible to diagnose a straightforward color defect in a matter of minutes.

(*7*) *Maxwell's Spot.* Walls and Mathews (1952) have used Maxwell's spot, the

entoptic projection of the macula with the aid of a purple filter, as a means of studying defective color vision. They reject the idea that the spot has its origin in absorption in the yellow macular pigment, and consider that it is due to the nonuniform distribution of the color receptors in the fovea and its immediately surrounding area. They found that protan subjects see the spot with characteristic colorings, whereas the majority of deutan subjects see no spot at all. The subjective nature of the observation probably makes it unsuitable as a routine test for color vision, but it may prove important as a supplementary test, especially in research work.

APPLICATIONS OF DIAGNOSTIC TESTS

Accurate methods of diagnosis are of such paramount importance to the medical profession in general that it might hardly appear necessary to argue their value for color vision in particular. Yet, since color defects are not normally associated with disease, the impetus for accurate diagnosis is likely to be scientific and vocational rather than clinical. I should like to illustrate this by reference to specific fields of study.

One such field is genetics. Many pedigrees of color defects have been published, and the transmission of the protan and deutan types of vision are well understood. If, now, reliable information could be accumulated about the degree as well as the type of deficiency, we could initiate a study of the evolution of the defect. It would, however, be useless to commence such an investigation unless we were quite confident that we could diagnose and grade the defects correctly. In the case of tritanopia, Kalmus, in his study of its transmission (Ann. Hum. Genetics, 1955, *20:* 39) depended quite vitally on the reliability of the tests he used, since excessive pigmentation can so easily be confused with tritanopia.

Allied to these studies is the question of the distribution of the various defects in the population, and the variation in their distribution with geographic location and with race. In the latter problem, it again becomes important to distinguish the effects of pigmentation from those of genuine color deficiency, and the test must be chosen with this in mind.

Another special field is the discovery and detailed study of defects which do not fall into any of the accepted categories. One hears fairly often of unusual types of color vision, but their apparent abnormality can generally be traced to the combination of an orthodox defect with some ocular characteristic such as heavy pigmentation, low light sensitivity, poor acuity, unusual adaptation or the like. On the other hand, a genuinely rare defect may be of immense interest and is most likely to be discovered in any mass survey if a critical diagnostic test is used.

One field of research which has received increasing attention recently has been the comparison of color vision in the peripheral retina with that at the fovea. An exhaustive study of this problem for even a single observer is very lengthy indeed on account of the large number of variables involved—retinal position, size of test field, illumination level, state of adaptation and surround illumination, duration of exposure, etc. If peripheral vision is in fact a form of defective color vision,

then much interesting information on a number of observers might be secured with comparative speed by applying suitably designed color vision tests. In this case, the tests would have to be designed to take account of the poor acuity of the peripheral retina, and also of the desaturating effect caused by the intrusion of rod vision.

There is also, of course, a clinical interest in peripheral vision. Indeed, the perimeter is used to good purpose by the ophthalmologist, yet the determination of the color fields represents a relatively minor and rather ambiguous aspect of peripheral color vision. More ambitious tests might well reveal additional information of much greater medical significance.

Comment: I heartily agree with Dr. Wright's opinion that even the clinical examiner (as opposed to the researcher) should do more than determine whether the subject before him is color normal or somehow color blind. The testee has every right to know the type and "degree" (subtype, rather) of his defect, and how he is probably seeing the world as compared with the color normal, and in what way he would be handicapped in any proposed vocation. Moreover, the prospective employer for whom the testing is being done can sometimes be assured that the candidate is safely employable in a particular job, in spite of a mild defectiveness. This does both applicant and employer a good turn.

I note only one error in Wright's characterizations of the serious defects (i.e., the dichromasies and the much rarer monochromasies). "Cone monochromats," whom I would call atypical achromates (totally color blind but with normal visual acuity), do not all have normal spectral sensitivity. Perhaps half of them have the luminosity curve of a protanope, and suffer a considerable reduction of the brightness of yellow, orange, and particularly red lights.

In my opinion, Wright overemphasizes the frequency with which unusually heavy lentine or macular pigmentation produces any simulation of (tritanoid) color blindness or ever causes a real defect to be misdiagnosed. Not being genetically minded, he overlooks the possibility that any unique case that seems hard to classify may represent the simultaneous inheritance of two defects.

Wright's evaluations of the tests he has selected to describe are quite fair. They are all practical clinical color *blindness* tests excepting the Farnsworth-Munsell 100-hue test, which is most cumbersome when used for this purpose; its greater usefulness is in helping to evaluate the color aptitude of color normal subjects. I am impelled to comment upon only two of the others:

The H. R. R. test is indeed the best of the confusion chart tests available to Americans, although the Swedish tests have been found to pass fewer defectives and mislabel fewer normals. For diagnosis however (as apart from dichotomous normal-abnormal screening) the H.R.R. is far from perfect. I have accumulated dozens of cases where it has "missed," and from these it is clear that the test tends to call deuteranoids medium or strong in defectiveness when they are not dichromatic (deuteranopic) at all, and tends to call protanopes (dichromatic protanoids) only medium in grade where their defect is certainly "strong." Dr. Rand herself is no longer sure that the "medium" plates in the test have any value. A red-green defective may be anomalously trichromatic (and can be called mildly defective), or he may be dichromatic (and has to be called seriously defective). There is nothing in between, for the so-called "extreme anomal" is not intermediate but has an unstable system which vacillates between anomalous trichromasy and dichromasy, making him the most dangerous of all in color identification situations. Wright is justified

in gently scoffing at the H.R.R.'s pretense of differentiating between "tritans" and "tetartans"; not, however, on the ground that tetartanopia is only "theoretical." It is very real, as the work of G. E. Müller is alone enough to prove; but, it is so very rare that the British investigators, particularly, tend to think that it is "tritanopia, studied with inadequate methods." The H.R.R. test is presumptuous, however, in requiring its purchaser to pay for a number of plates he will never need. There is no such thing as "medium tetartan" color deficiency. Only one "strong tetartan" (tetartanope) was ever described for the whole of North, Central and South America, and he is now dead.

The Nagel anomaloscope was so named because it was offered for the detection of protanomals and deuteranomals. One can use it for much more than this, as Wright says. How much more, he does not entirely bring out. With an anomaloscope and a white light box (but not with any other devices) one can identify the very important "extreme anomal" and differentiate him from the stable anomal and the stable dichromate. The protanope and deuteranope are easily distinguished, though not in the way Wright describes. The protanope cannot put any more red light into the field than the deuteranope can, when each is demonstrating that he can color match the yellow to the red end of the red-green scale. The protanope gives himself away by using a feeble yellow to match the pure red light, because the latter looks so dim to him.

To what Wright quotes from Nelson (1938), there can be added confirmation from recent work by Hurvich and Jameson. The extent of the range of red-green proportions over which the anomal gets an acceptable match for the standard yellow, and the departure of the mean of that range from the normal's mean setting, are unrelated. The anomal's mean setting may show how much the various hues are displaced to longer or shorter wavelengths in his personal spectrum. But his matching range, if narrow or wide, shows how little or how much his hue discrimination is inferior to normal, and this is what matters in his everyday vision. The anomal's hue discrimination, in turn, is poor because the really central feature of his color vision is a general depression of saturation (color strength). A further expression of this is that there has to be more coloration in a light or dark object than a normal readily sees, before the anomal perceives anything but a light or dark gray. This is why he fails on the earlier plates in the H.R.R. test.

Wright deplores the high cost of the Nagel anomaloscope (about $1,000.00 in this country) and the fact that it will detect only protanoids and deuteranoids. This is what really leads him to say that no single device will do for all-around diagnosis excepting his own precision tricolorimeter, which is out of the question. He advocates the Nagel, plus at least one paper test capable of catching tritanoids. But even the Nagel could be afforded only by a clinic or a particularly well heeled private practitioner.

There is an inexpensive way out. While the classical Rayleigh equation employs monochromatic red and green lights mixed to match a monochromatic yellow, there is no reason why the lights in an anomaloscope must be monochromatic and produced with an expensive Amici prism. This has been proved by every one of the many successful homemade anomaloscopes which have been built in this country. Such an anomaloscope need not cost even as much as an H.R.R. test together with the special illuminant prescribed (which costs more than the test itself). Sadly, no optical manufacturer has placed a cheap filter anomaloscope on the market—perhaps because any good optical designer, given the problem, would have to say that he saw no excuse for putting any "optics" (lenses, prisms, mixing cubes, polarizers) into the thing at all.

All that is required is a white-enamel lined box with a lamp (60 watts will probably do) at the back end behind a transverse partition with two windows in it, a red and a green gelatine filter edge-to-edge in a vertical slide which the turning of one knob moves across

one window, a yellow filter and an opaque area in a second slide which another knob moves across the other window, and a lengthwise partition ending in a bit of black paper the thickness of which separates two small semicircles of ground glass forming the viewing field at the front of the box. If now the red filter can be replaced by a blue one and the yellow can be either simply removed or replaced by a blue-green, the instrument with the R + G = Y equation will sort out the protanope, deuteranope, protanomal, and deuteranomal; with the R + G = White equation it will detect the rare tritanope; and with the B + G = BG set of filters it will identify the even rarer tritanomal. The totally color blind can make a match with any set of filters, with the two filter slide set anywhere. But he does not know what the word "color" means, and unless he is a child he tells *you* that he is totally color blind. No test is needed to worm the information out of him.

The filters chosen for the regular equation (R + G = Y) must meet one important requirement. While any protanope or deuteranope will obtain a *hue* match between any yellow and any mixture of any red and any green, he will be able to match at only one place on a red to green scale that has a gradient of saturation. This will make him appear to be an anomal. The colors of the filters must be equal in *saturation* for the dichromate if he is to differentiate himself.

A set which should work well: for the red, two layers of Wratten No. 29; for the green, No. 15 superimposed on No. 61; for the yellow, No. 73 (which is greenish, but this does not matter). Unless the climate is humid, these may be bought as cheap 2 by 2 inch gelatins and bound between lantern slide covers with narrow Scotch tape. The red-green window will need to be narrowed with opaque material by trial and error until neither the red nor the green light is quite as bright as the full yellow. It does not matter whether the red and green are equal in *brightness*.

The viewing field should not subtend more than 2 degrees at the eye of the testee. If his arms can rest on the table and he can operate the knobs on the front of the box at arm's length, a 2 cm. field will be about right and not so small as to be hard to contrive. Scales can be provided by having each slide push an indexed rod up and down through the top of the box, against a 2 inch piece of cheap millimeter ruler mounted vertically on the box.

GORDON L. WALLS

DESCRIPTION OF AN OPHTHALMOSCOPE FOR EXAMINING THE RETINA IN THE LIVING EYE

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Original monograph, "Beschreibung eines Augen-Spiegels zur Untersuchung der Netzhaut im lebenden Auge," Berlin, A. Forstner, 1851
Based on the translation by Robert W. Hollenhorst, M.D., A. M. A.
Arch. Ophth., 1951, *46:* 565–583

This publication contains the description of an optical instrument with which it is possible accurately to observe and examine the retina. To be of value, such an instrument must overcome two important problems. First of all, as we observe the normal eye its anterior appears to be completely dark. The reason for this is that under ordinary circumstances the refractive media of the eye prevent us from observing illuminated portions of the retina through the pupil. Only by looking through the refractive media can we visualize the background of the eye. It is necessary to have a special procedure for producing the illumination, as well as an optical instrument which will allow the observer's eye to focus sharply on the retinal structures.

ILLUMINATION

This black reflex is not a property of the choroidal pigment. Even though the pigment layer could completely absorb the incident light, as do some other black substances, there are tissues present which could reflect a considerable portion of the incident light and thus become visible. This is especially true of the retina. It is even truer of the blood vessels of this tissue, since their branches carry sufficient blood to give them a definite reddish hue. Also, in the fundus of the eye there is a shining white area, the position of entry of the optic nerve, upon which there is no pigment; therefore, it reflects all light which falls upon it.

That it is the refraction of light in the ocular media and not the color of the background which causes the black reflex of the pupil is readily demonstrated by means of simple experiment. For this purpose one can use a small camera obscura with a thoroughly blackened interior, really an artificial eye, and at the site where the image is projected one can place an opaque white panel, such as a piece of thick white drawing paper. If an attempt is made to peer through the lens from any angle whatsoever the interior of the instrument appears to be completely dark. If the convex lens is then removed, or if the distance between it and the sheet of paper is changed materially, the observer can readily visualize the white surface of the paper.

HERMANN VON HELMHOLTZ

(1821–1894)

How can refraction of light produce this phenomenon? When light from a luminous point is allowed to fall on a suitably accommodated eye, a small part of it is reflected from the neural elements and blood vessels and a part from the layer of rod shaped cells. As was shown by E. Brücke, the light which returns from the latter structures passes again through the pupil, without being dispersed to other portions of the interior of the eye. The returning rays traverse exactly the same path, but in the opposite direction, as that used in converging

upon the retina through the refracting surfaces of the eye. The angle of incidence of the departing ray is identical with the angle of refraction of the entering ray at the limiting surfaces of the medium. If we designate *a* as a luminous point outside the eye and *b* as its image at a point on the retina, we find that the ocular media focus the emergent rays from *b* once again into an image at *a*. The image of the illuminated point on the retina thus coincides with the original luminous point. Hence, all the incident light which is reflected must return to its origin and can never take another direction. Therefore, it is impossible to visualize the illuminated portions of the retina without special equipment. Furthermore, we cannot bring our eyes into the pathway of the returning light without completely interrupting the incident rays.

Up to this point we have assumed that absolutely sharp images are formed in the eye that is being observed. When this is not the case, the foregoing propositions are not universally applicable, and the reflected light may largely return to the luminous object. However, a portion of the reflected light may pass by, so that an observer who is situated very near to the line of direction of the incident light may be able to perceive a portion of the reflected light. This fact forms the basis for the methods of Cumming (Tr. Med.-Chir. Soc., London, *29:* 1845–1846, 283) and Brücke (Arch. f. Anat., 1847, 225) for observing the illumination of human eyes. From what has been said, it is evident that the less exactly the rays emanating from a luminous point are focused on a point on the retina, the more intense the illumination will be. However, in these investigations it is possible for the observer to perceive only a small fraction of the returning light. In fact, he sees only those irregularly refracted rays which are of no use in the production of a definite image. For our purpose another method must be employed to make it possible to peer into the eye in exactly the same course as that of the incident light, and not merely approximately in this direction. The means whereby this could be done was discovered accidently by von Erlach and investigated by Brücke. Von Erlach, who wore spectacles, noted that the eyes of a friend would be illuminated if the latter looked directly at the image of a light reflected in the lenses of the spectacles. Unmounted lenses also could be used as illuminating mirrors, and the observer likewise could see through these into a subject's eyes. We employ exactly the same procedure, but advantageously replace the spectacle lenses with carefully ground plane lenses.

In a darkened chamber containing only a single light source, we can set a small plane glass plate in such a position that the subject can see the reflected image of the light, although he need not look directly at this reflection. Light is thus directed into the subject's eye from the anterior surface of a lens, and the observer can simultaneously examine the eye through this same lens without being aware of the light reflected from the anterior surface. It is evident that in this way it is possible to direct the line of vision into the subject's eye in exactly the same direction as that of the course of the light. Under such conditions, the observer's eye will receive light from the depths of the other eye, and the pupil will be illuminated.

With my method, the entire light is used, with the exception of the portion

which is lost by passage through the reflecting glass. Moreover, the strength of illumination varies according to which portion of the retina receives the image of the flame. If it falls on the optic disk, most of the light is reflected, and the pupil is illuminated with a bright yellowish white light. The retina proper, however, reflects much less light, principally red light. In general, the image of the flame is stronger the nearer it is to the optic disk, and weaker the farther away it is from this disk. On the contrary, the yellow macula, the site of direct vision, which is used when the observed eye gazes directly at the reflected image of the flame, returns much less light than do the neighboring structures.

In order to fulfill the condition that the observer gaze into the eye exactly in the direction of the incident light, the glass plate can be adjusted by the observer. This method requires that the subject's face be shaded and the reflecting plate be made so small that it is just large enough to see through. The reflected light then will appear upon the shaded face of the subject as a small bright spot of about the shape of the reflecting glass. The observer must aim this bright spot in such a way that its center falls on the subject's eye, while he himself peers through the lens. In this way the lens may be aligned very easily, and the subject's eye can be turned to all sides without much difficulty, to permit the image of the flame to fall upon various parts of the retina.

The same simple method can be utilized advantageously to illuminate any dark cavity with a narrow opening, such as the auditory meatus or the nose. To visualize the tympanic membrane, the subject must be placed with his back against a window, preferably in sunlight; the auricle must be drawn slightly backward, and the reflected light must be directed into the auditory meatus while the observer looks in through the lens. Thus it is possible easily and conveniently to illuminate the drum head to any degree desired for purposes of examination.

If it is desired to examine closely the structure of the retina one must attempt to get as bright a light as possible. This objective can be reached in two ways, either by properly adjusting the angle made by the incident light or by increasing the number of the reflecting plates. If several reflecting surfaces are arranged parallel and one behind the other, and the illuminated surface is large enough that the reflected images which are produced by the various mirror surfaces superimpose themselves upon the observed eye, the various images are combined into one of greater brightness. By calculating the amount of light reflected back and forth between the various surfaces, it is possible to determine the total amount of light reflected in any system of parallel surfaces. The returning light re-enters the mirror system and divides into a part which is again reflected and a part which penetrates the system. Only the latter portion enters the eye of the observer. A value deviating slightly from the foregoing maximum is obtained if the light is reflected from one glass plate at an angle of about 70 degrees, from three plates at an angle of about 60 degrees, and from four plates at an angle of 55 degrees. These positions, therefore, are approximately the most efficient.

It is important to consider that a small portion of the light which strikes the eye of the subject is reflected from the cornea and appears to the observer as a

pale light spot in the field of vision. This spot is situated in the center of the pupil of the subject directs his eye straight at the mirror and if he looks directly at the reflected image of the flame. It is of distinct advantage to the observer of the intensity of the corneal reflex can be considerably diminished. This reflex appears to be much less prominent when four plates at an angle of 56 degrees are used than when either three plates at a 60 degree angle are employed, or one plate at a 70 degree angle, although the retinal image previously described retains practically the same intensity of illumination. Even with variation in the number and position of the plates, the apparent brightness of the corneal reflex is not proportional to the brightness of the retinal image because the light which enters the eye of the subject is partly or entirely polarized by reflection and becomes depolarized by diffuse reflection from the retina. This is a phenomenon which does not occur in the case of the specular corneal reflection. Therefore, from every point of view, the necessary intensity of light is more readily obtained by increasing the number of plates (since they reflect the light below the polarization angle of 56 degrees) than by increasing the angle of incidence because the corneal reflex can be entirely avoided by greatly multiplying the number of plates.

FORMATION OF A CLEAR IMAGE OF THE RETINA

The problem of widening the field of vision makes it imperative that the observed and the observing eye be brought as close together as possible. It is possible, with less magnification, to permit the greater part of the visual field to be maximally illuminated; on the contrary, if greater magnification is used, this may not even take place in the center. Even though a higher magnification would be very advantageous, it is not possible to make use of it, since the illumination decreases so greatly. Moreover, the living eye cannot be held sufficiently quiet for good fixation of various parts of the image, as would be necessary if higher magnification were used. The visual field is next to be considered. That part of the retina which can be seen becomes smaller the farther the observer is from the subject's eye, and becomes greater when the observer is nearer.

DESCRIPTION OF THE OPHTHALMOSCOPE

In order to begin observations, as described above, it is convenient to combine the mirror and a concave lens in a suitable frame. I have chosen the name Augenspiegel for this combination because of its analogy to similar instruments of this name. Good blackening of the nonreflecting surfaces is essential. First of all, the inner surface of the ocular piece must be blackened and the observer must press his eye as closely as possible into the ocular piece in order to exclude all extraneous light which might come from the flame onto these surfaces. Second, the bare metal parts which are directed toward the observed eye must be blackened so that they will not produce disturbing corneal reflexes. To use the instrument, the observer places the subject in a darkened room near the corner of a table upon which a well burning double draft lamp is set at the same level as that of the eyes lateral to the face. It is advantageous to place on the table, at a suitable visual distance, a dimly lighted object upon which the eyes of the subject

can fixate at definite points; an example would be a blackboard divided into quadrants, each of which is designated by a number. Then, if the eye is permitted to fixate the various quadrants one after the other, the image of the flame will fall on different portions of the retina, which then may be investigated by the observer in any order desired. The observer is seated in front of the subject. Without first looking through the ophthalmoscope, he directs it in approximately the right direction, whereupon a brightly illuminated spot is cast on the face by the reflecting surface. Then the mirror is turned in such fashion that the middle of this illuminated spot falls on the eye, and if the axis of the instrument is correctly aligned, he looks through. If the retina is not seen clearly, but the pupil appears illuminated, a different concave lens must be employed. An observer who has trained himself to alter voluntarily the accommodation of his eyes can easily determine whether he sees more clearly with far-sighted or with near-sighted accommodation and whether he therefore needs more or less strongly curved lenses. As with all optical instruments possessing a focusing device, it is necessary in the use of this one to accommodate the eyes for infinity and then to adjust the instrument to the eye.

VISUALIZATION OF THE RETINA AND THE IMAGE OF THE FLAME

If one is desirous of examining the retina thoroughly, it is necessary, as mentioned previously, to erect a numbered blackboard to use as a fixation point for the eye of the subject. If he continues to follow the course of the vessels in the direction of the larger branches, he approaches finally the place of entrance of the optic nerve. This structure is distinguished from the rest of the background of the eye by its whiteness, because it is not covered by pigment or a fine vascular network; instead, the white cross section of the nerve lies quite free, at most penetrated by a few fine vessels. Usually, the arteries and veins of the retina arise from the medial portion. Occasionally, one can see a portion of the vessels still buried in the substance of the nerve and can appreciate that this substance must be very strongly transparent in the living state. It is possible to distinguish the two types of vessels, one from the other, by the brighter color of the blood and the double contour of the walls of the arteries and their first branches. I have not been able to observe pulsations with certainty. The first main branches of the vessels border the optic nerve on the inner side and later branch out, above and below, over the expanse of the retina. The appearance of the sharply demarcated red vessels upon the bright white background is of surprising elegance.

In other parts the background of the eye looks red; here are seen larger and smaller blood red branching vessels, which may be clearly distinguished from the background. The background itself appears not to be entirely homogeneous, but indistinctly reddish. This seems to arise from the fact that the narrow capillary network is too delicate, is illuminated too faintly, and is too transparent to be clearly distinguished from the underlying light gray tissues of the retina. That the background in the vicinity of the optic nerve appears to be brighter may well be due to the fact that here the retina is thicker, as a consequence of the superimposed layers of the nerve fibers; it is always thinner toward

the periphery. The site of direct vision (the yellow spot) is especially well distinguished from its immediate surroundings. In order to bring this spot into view, the subject's eye must gaze directly at the reflected image of the flame. In such a view the retina appears to be much darker; also, no traces of any capillary vessels are visible upon it. In observing this site, however, one is very much disturbed by the corneal images, which are situated exactly in the center of the field of vision, whereas when more lateral portions of the retina are examined these reflexes are situated somewhat more to the side.

After one learns to recognize the characteristics of the retina in the normal eye, I have no doubt that it will be possible to diagnose all the pathologic conditions of the retina by visual observation, as is done in examination of other transparent parts, such as the cornea. Engorgement of the vessels or varicosities of the vessels can easily be perceived. Exudates in the substance of the retina, or between the retina and the pigment layer, can be recognized by their light appearance against the dark background, similar to what can be seen in corresponding lesions in the cornea. If they are situated partly in front of the retina, the blood vessels will be hidden as by a veil. In this respect, I recall that, according to Brücke, the living retina is almost as transparent as the other ocular media. Fibrinous exudates, which are much less transparent than the ocular media, must therefore considerably increase the reflex if they are situated in the fundus of the eye. I also believe that opacities of the vitreous body will be recognized much more readily and exactly. It is easily possible to estimate the extent of the opacity by means of the degree of blurring of the retinal vessels. If scintillating particles have become detached from such an opacity, these also may be perceived readily. In short, I believe I do not exaggerate when I anticipate that all those changes in the vitreous body and the retina previously noted in cadavers will be recognized in the living eye. This fact appears to offer the greatest impetus to development of the pathologic study of these structures.

Moreover, it is possible, when it is necessary to do so, easily to determine objectively the presence and the degree of myopia or hyperopia of the observed eye. The observer should first examine a normal eye. He should allow this eye to fixate objects at various distances and should note which concave lenses are needed at the various stages of accommodation of the eye. Then, in investigating another eye, he can determine, by the strength of the concave lens needed to give a clear view of the retina, the state of accommodation of the subject's eye. The observer is thus entirely independent of the statements of the subject, since he himself can see, as though with the other's eye, the refractive media of this eye. In this way, for example, I was able to examine a completely amaurotic eye and determine that this eye was highly myopic as well.

These investigations led me to an important physiologic deduction. The isolated cross section of the optic nerve evidently is so transparent that light falling upon it can penetrate deep into the substance of the fibers, inasmuch as at times the tortuous loops of the central artery and the central vein can be seen shimmering through the substance of the nerve. If the image of the flame is cast upon the site of entry of the optic nerve, all the nerve fibers, or at least a very large portion

of them, are exposed to more or less intense light, and yet apparently no light is perceived. We must, therefore, conclude that the fibers of the optic nerve are insensitive to objective light, although every other kind of stimulation is perceived as subjective light. It is not difficult to make the assumption that all stimuli which are able to act on the visual nerve system produce sensations of light, but that the vibrations of the ether are able to act only on the retina. This similar situation may be noted in the reaction of the nerves of touch to warmth and cold. In this case as well there is a different response in the peripheral ramifications than there is in the trunk. Furthermore, it is possible to conclude that in the retina it is the cellular elements which are sensitive to light, and not the nerves which radiate over the inner surface. We are able to postulate further that the continuations of the visual nerve fibers in the retina are insensitive to light.

Comment: No instrument has developed ophthalmology as much as the ophthalmoscope. It stimulated likewise the progress of other fields of medicine by inspiring other endoscopic instruments. The ophthalmoscope was first publicly presented by Helmholtz before the Physical Society in Berlin on December 16, 1850. In acquainting his father with the discovery, Helmholtz wrote: "Formerly a number of ocular diseases were designated 'black cataract,' as the changes in the living eye were not understood." Von Graefe, who realized the immense practical importance of the invention, in a letter to Helmholtz said: "Forgive one not known to you an inquiry about a subject of the greatest personal interest. Professor Brücke told me of your success in constructing an instrument which permits the examination of the living retina. I am anxious to try this much longed for diagnostic instrument and beg you to send to Berlin one or two constructed according to your specifications." The Helmholtz ophthalmoscope was rapidly modified. In 1852, Reute improved the illumination by using a concave mirror with a central perforation and also evolved the indirect method of ophthalmoscopy. In the same year, Rekoss, Helmholtz's instrument maker, added movable disks bearing a battery of lenses which facilitated the inspection of the fundus and permitted a rough determination of the refraction. The first practical ophthalmoscope, designed for the measurement of refraction, however, was that of Loring in 1869. With its use the general employment of an objective method for the determination of refractive errors was initiated. In 1873 Cuignet observed that at a distance of 1 meter the apparent movement of the illuminated area depended on the refraction of the eye and utilized this phenomenon as an objective test. In 1878 Mengin christened the procedure "retinoscopy" and Landolt explained the optical principles involved. By 1870 the fundus pictures revealed by the ophthalmoscope were incorporated in atlases by Sichel, Eduard von Jaeger and Richard Liebreich. An atlas of the comparative ophthalmology of mammals by Lindsay Johnson appeared in 1897 and of the fundus oculi of birds by Casey Wood in 1917. The modern period of ophthalmoscopy has been marked by refinements of the electric ophthalmoscope, first introduced by Dennett in 1885.

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Biographical Notes

Hermann von Helmholtz (1821–1894) was born at Potsdam, Germany. His father was a teacher of classical languages; his mother was Caroline Penne, a descendent of William

Penn, founder of Pennsylvania. He received his medical degree in 1842 from the Royal Friedrich-Wilhelm Institute where he made firm friends with Brücke, du Bois-Reymond and Ludwig. In 1849 he became professor of physiology at Koenigsberg and while preparing his lectures conceived the idea of the ophthalmoscope. After occupying similar chairs at Bonn and Heidelberg, he was appointed director of the Physical Institute at Berlin. In 1893, at the request of Hermann Knapp, von Helmholtz attended the World's Fair at Chicago. On his return home he suffered a serious fall aboard ship and died the following year.

Helmholtz ranks as one of the greatest scientists of all time. Like Thomas Young, he preferred research to medical practice; and like Young, his important contributions to vision and optics were but facets of a manifold interest. His works on acoustics, nerve conduction, electro- and thermodynamics, and the conservation of energy (written independently by Joule and Robert Meyer) were equally fundamental. His writings inspired Hertz to search for Maxwell's electromagnetic waves, an investigation that led Marconi to the invention of wireless telegraphy. In 1890, in an address commemorating the 600th anniversary of the medical school at Montpellier, he said: "No one can work scientifically without aiding his country and, at the same time the entire civilized world." The last edition of his *Physiologic Optics*, edited by Gullstrand, von Knies and Nagel, was translated into English by the American Optical Society in 1924.

REFERENCE

KOENIGSBERGER, L.: *Hermann von Helmholtz*. English translation by F. A. Welby. Oxford, Clarendon Press, 1907.

Book Reviews

"Gifford's Textbook of Ophthalmology," by *Francis Heed Adler (W. B. Saunders Co., Philadelphia, Pennsylvania. 499 pp., 277 figures, and 26 color plates, $8.00) is the sixth edition of a standard textbook directed to the general practitioner and the medical student. It is reviewed here by Bernard Becker who is Professor and Head of the Department of Ophthalmology at Washington University, St. Louis, Mo.*

The teaching of ophthalmology in medical school proves most rewarding and is best received when it is presented from the point of view of the student. When one comes to appreciate the wisdom of this approach, *Gifford's Textbook of Ophthalmology* affords an ideal supplement to the course. In this book, emphasis is placed on the information and technique of examination the student needs in his daily work as well as in his later life as a general physician. The recent revisions of the text have enlarged upon this approach and brought the material up to date in a most lucid fashion. In addition, the wealth of clinical information, the extensive knowledge of current research and the vast teaching experience possessed by the author have added immeasurably to the value of the book.

As with any textbook it is possible to find statements or points of view expressed which may not satisfy the individual teacher. Thus, the classification of epidemic keratoconjunctivitis under "allergic forms of conjunctivitis" seems inappropriate; the discussion of acute angle closure glaucoma under the heading "chronic simple glaucoma, closed angle type," tends to confuse the student as to classification; and the suggestions for the use of fluorescein solutions for staining the cornea could perhaps contain a warning about possible contamination and the preferential use of fluorescein paper. However, with each edition it becomes increasingly difficult to find even minor inadequacies of the text. The gathering of information on ocular injuries into one chapter should prove most useful to the busy intern or practitioner.

To one who was brought up on this text and has since used it extensively for teaching medical students, the present revised edition is most welcome. It is recommended enthusiastically to the teacher, student, and practitioner, not just as a book for their library, but as a ready reference for their desk.

"The Problems of Vision in Flight at High Altitude" by *Thomas C. D. Whiteside (Butterworth's Scientific Publications, London, 162 pp., 64 figures, $5.00) is a physiologic study of the ocular problems presented when the bright blue sky is below and the dark blue sky above is optically empty. It is reviewed here by Frank W. Newell.*

Flight at high altitude refers in general to flight in the stratosphere and in practice refers generally to flight above 40,000 feet. The earliest visual problems of flying arose from lack of oxygen and the author credits Wilmer and Berens

with the initial physiologic recognition that the eyes were affected by altitude because of lack of oxygen and not because of reduction of barometric pressure.

In the early 1920's transient loss of vision due to blackout (failure of vision due to increased centrifugal force) was noted by pilots in the trophy races. During World War II visual problems involved air-to-air search, visual acuity, judgment of distance, anoxia, glare and the development of flying goggles.

The high speed of modern aircraft gives rise to new visual problems, with the pilot flying blind since the distance at which he can see another target expressed in time may be less than his reaction time. Vibration of the aircraft at low altitude may cause the eye to vibrate at its natural frequency with visual interference which may also occur in passing through the speed range from subsonic to supersonic speed.

The visual problems of high altitude arise from two principal factors. The first is the reversal of light distribution so that the bright blue sky formed by cloud and haze is below the observer and the darker blue sky is above. Under these conditions adventitious light from below floods the eye and casts a troublesome haze over the entire visual field. This glare causes difficulty in regard to visibility in the cockpit and is accentuated by anoxia.

The second factor is the clear blue sky without a trace of a cloud which constitutes an empty visual field. This empty field gives no sensation of depth or of distance; in consequence a conscious effort to focus in the distance may result in focusing even nearer to the resting position. Under these conditions, the pilot searching the sky may suddenly realize that his eyes are focused not in the distance but on spots of dust on the windshield. Even if the pilot does recognize an object, judgment of its distance, size, and relative speed is impaired by absence of clues from parallactic displacement in the cloudless sky.

The author, a physiologist, discusses in detail the problems arising from glare and from visually empty space in a relatively nontechnical manner. The book is certainly not intended for the practicing ophthalmologist and concerns problems the solution of which is related to aircraft design, radar and the like. However, for those who enjoy a diversion into the fantastic world of tomorrow and an outline of problems in visual physiology of aviation medicine, and for investigators in the fields of refraction, accommodation and optics, the book is highly recommended.

"The Year Book of the Eye, Ear, Nose and Throat (1956–1957)" by *Derrick Vail and John R. Lindsay (The Year Book Publishers, 448 pp., 128 illustrations, $7.00) abstracts some 168 ophthalmic articles and a nearly equal number of ear, nose and throat articles.*

The Year Book is familiar to nearly all ophthalmologists and otolaryngologists as an annual source of what is new, interesting and significant. This volume equals the standards established by earlier editions and offers a useful compendium of the world literature in the field which appeared between October 1955 and September 1956. A most welcome announcement is that next year the year book is being divided into separate volumes—a *Year Book of Ophthalmology* and a *Year Book of Ear, Nose and Throat.*

Ophthalmic Meetings

THE OXFORD OPHTHALMOLOGICAL CONGRESS 1957

The Forty-Second Oxford Ophthalmological Congress was held in Oxford on July 1, 2, and 3, 1957. The current master, Sir J. W. Tudor-Thomas, opened the meeting with an address of welcome to the members and their guests. Men members of this congress are usually accommodated in one of the Colleges of Oxford University; this year Balliol College were the hosts. Each morning at 7:30 a bathing parade started from the porters' lodge for Parson's Pleasure, a spot famous amongst undergraduates for its bathing facilities. The annual golf competition was held on the evening of the first day; at the informal dinner afterwards a penalty for the absence of the club tie was a fine of a round of drinks from the offending golfer.

In 1909, Robert Doyne laid the foundations for the Oxford Ophthalmological Congress. One of the founder members was a man named Vail. This year the Doyne Memorial Lecture was delivered by this surgeon's son, Dr. Derrick Vail, M.D., D.O. (Oxon) F.A.C.S., F.R.C.S. (Hon) from Chicago. Dr. Derrick Vail is no stranger to British ophthalmologists; he was director of ophthalmology to the United States Forces in Europe during the last World War. Dr. Vail said that the first time he was present at the Oxford Ophthalmological Congress was in 1930 when Harry Friedenwald gave the Doyne Lecture, and he reminded his listeners that the untimely death of Jonas Friedenwald prevented him from following in his father's footsteps by delivering the 1956 lecture.

The subject of Dr. Vail's talk was the zonule of Zinn and its clinical significance with particular regard to cataract extraction. He had some beautiful photographs of the ligamentous connections of the lens capsule and he demonstrated very vividly an attachment of the lens to the anterior vitreous face.

The first subject of the meeting was a discussion on the facial neuralgias. Mr. E. F. King (London) classified the neuralgias and spoke on the problems confronting the ophthalmologist. He mentioned that periostitis of the orbital walls was a condition of which to be aware when searching for a cause of obscure ocular pain. The neurologist's approach to the problem was discussed by Dr. W. Ritchie Russell (Oxford). This speaker felt that postherpetic neuralgia may be relieved by treating with local anesthetics, or better still by percussion therapy, the hyperesthetic areas bordering on the affected surfaces; he emphasized the importance of the psychologic approach and would impress upon the visiting relatives that they should not discuss the pain with the patient.

Mr. G. F. Rowbotham a neurosurgeon from Newcastle, England, considers it criminal to withhold surgery in tic douloureux. He discussed treatment by injection, neurectomies in the face, and intracranial operation.

Professor Marc Amsler from Zurich followed with a talk on the value of photography in tracing the course of disease.

The afternoon session was opened in stimulating and light hearted fashion by Mr. J. Horton Young from Nottingham, who discussed the successful removal of a cataractous lens through an incision in the pars plana ciliaris. Mr. Young considered that for an important congress such as this he had better produce a second case; this he did.

Mr. A. G. Leigh (London) and Mr. J. W. Ridge (Bristol) then discussed some problems of the preservation of corneal tissue by freezing. The concensus of opinion on this subject appears to be that frozen material is legitimate for use in lamellar grafts but not in perforating grafts because the damage sustained by the endothelium in the freezing process is a primary cause of postoperative opacification.

Dr. Howard Reed and Dr. J. E. L. Bendor-Samuel (Winnipeg) discussed the detection of glaucoma before evidence of visual impairment. Their investigations supported the view that approximately 2 per cent of glaucoma cases are missed by not performing routine tonometry.

Mr. Rupert Parry (Cardiff) reported on an investigation into the longterm end results of concomitant strabismus.

The final item on the first day was a paper by Mr. P. D. Trevor-Roper (London) on hypothermia in hamsters and the ocular response to freezing and resuscitation. The only major ophthalmic change noted was the development of subcortical cataract and the occurrence of corneal edema.

For nongolfers a garden party, to which wives and friends of members were invited, was held in the grounds of Balliol College at the end of the first day's afternoon session.

On Tuesday Mr. Harold Ridley from London opened proceedings with a talk on the results of fundus photography with the new Zeiss camera. Many members present favored the older Zeiss Nordenson instrument.

Dr. G. Meyer-Schwickerath (Bonn) followed up his fascinating lecture delivered in Dublin last year by reporting on further progress in the field of light coagulation. In the words of the deputy master, Mr. O. M. Duthie, who was chairman, this was one of the great lectures of the meeting and one left the meeting with the feeling that he had with him something out of this world. The lecturer gave an illustrated report on 560 cases treated by light coagulation. The report shows that besides the sealing of retinal tears the following indications become more and more important: (1) intra- and postoperative treatment; (2) treatment of tumors of the fundus (melanosarcoma, retinoblastoma, angiomatosis and metastatic tumors); (3) treatment of proliferative retinal vessels; (4) treatment of inflammatory diseases; (5) coagulation of the iris to produce a new pupil; and (6) coagulation of tumors of the iris and skin.

Following the delivery of the Doyne Memorial Lecture and the presentation of the Doyne Medal to Dr. Derrick Vail it was announced that the Sir Norman McAlister Gregg prize and medal had been awarded to Dr. Maurice Langham; since Dr. Langham was in America the presentation could not take place but the Congress wished to convey to him its congratulations.

After lunch Mr. B. W. Rycroft (London) spoke on the treatment of congenital ptosis, enumerating the various types of operation and discussing their merits and indications.

Dr. Edmund B. Spaeth from Philadelphia in a paper entitled "The Treatment of Monocular Aphakia" encouraged the use of contact lenses after extraction in patients with monocular cataract.

Mr. Harold Ridley pointed out that the aphakic spectacle correction gave a magnification of 22.2 per cent as opposed to 11.1 per cent with a contact lens and 7.4 per cent with an acrylic lens in the anterior chamber, whereas an acrylic lenticulus behind the iris gave no increase in magnification.

The remainder of the second day's scientific session was devoted to an "any question" hour. Amongst the interesting problems presented were the indications for corneal grafting at various ages. Mr. Leigh felt that 17 years was the minimum age at which a graft should be attempted. The sterilization of tonometers was another question put forward; flaming in the spirit lamp appeared to be the most satisfactory method available, but even this was not considered ideal.

A garden party at Holywell Manor preceded the Annual Dinner of the Congress in the Hall of Balliol College.

The final session of the meeting on Wednesday morning commenced with a discussion of the rehabilitation of the blind and partially sighted. Dr. Dorothy R. Campbell discussed these particular problems: (a) the adolescent with potential blindness; (b) the partially sighted adult worker; (c) the aged blind. Mr. T. D. Drake (a blind person who is Principal of Manor House R.N.I.B. Rehabilitation Centre, Torquay) gave a description of the 13-week training courses which are carried out at Manor House and American Lodge, Torquay. He said that cases of traumatic blindness are relatively easy to deal with but others may present a big psychologic problem.

Professor W. J. B. Riddell (Glasgow) spoke on the special problem of the deaf blind. Others to take part in this discussion were Mr. P. McG. Moffatt (London), Mr. T. M. Tyrrell (London), and Mr. H. Campbell (Wolverhampton); the latter surgeon showed some remarkable films demonstrating the independence created in blind persons by proper education and the high degree of skill in managing machinery which the blind worker can develop.

Sir Henry Holland expressed the wish that the administrators and blind welfare workers in Pakistan, where there is a tremendous blind problem, could be made aware of the wonderful progress in the rehabilitation of the blind in Britain.

Mr. J. E. H. Cogan (Tunbridge Wells) spoke on the advantages of phakoerisis and presented a film in support of his views.

The final paper of the meeting was on parabolic projection in visual field examination, by Mr. R. Pitts Crick of London. Standardization of conditions and recording as a parabolic projection were a great need. A mechanical parabolic attachment for the Lister perimeter would make it possible to record both the perimetric and central field findings for both eyes on the same chart.

This concluded the more serious proceedings of the Congress, but there were those who stayed to enjoy the beauty of Oxford and its ancient buildings or to

avail of the watering and sunbathing facilities of Parson's Pleasure, which was a popular spot in the hot July sunshine.

F. D. McAuley
Dublin

JAPAN OPHTHALMOLOGICAL CONGRESS 1957

In Japan three main meetings are held for the ophthalmologists every year. The first is the Japan Ophthalmological Congress, the second is the Clinical Ophthalmological Congress and the third is the Postgraduate Training Course. The Sixty-First Japan Ophthalmological Congress was held this year in Gifu City of Middle Japan, May 17 to 19. Approximately 2,000 Japanese and 14 foreign ophthalmologists attended this congress. The chairman was Prof. Shin-ichi Shimizu of Gifu Medical College. Eighty-nine reports and two special addresses were presented by Japanese members and seven addresses by authorities from The United States, Germany, France, China and Australia. Several speeches which were of special interest to the writer will be introduced here.

Prof. Noboru Kunitomo and others (Nihon University, Tokyo) presented a new classification of trachoma, shown in table 1.

McCalan's classification, which neglects acute trachoma, and the classification of the World Health Organization (WHO) are not very satisfactory for Japanese ophthalmologists who see various types of trachoma every day, but the classi-

TABLE 1

Classification of Trachoma

Acute stage:	
Tr.I(A)	Subacute Tr. Type A
Tr.I(B)	Subacute Tr. Type B
Tr.I′	Acute Tr.
Chronic stage:	
Tr. IIf	Trachomatous inflammatory signs (TIS) mainly localized on the fornices
Tr. IIft	TIS diffusely spread on the fornices and tarsal conjunctiva
Tr. IIt	TIS mainly localized on tarsal conjunctiva
Tr. IIIf	Cicatrix coexistent with Tr. IIf
Tr. IIIft	Cicatrix coexistent with Tr. IIft
Tr. IIIt	TIS coexistent with cicatrix and localized mainly on tarsal conjunctiva
Residual stage:	
Tr. IV	TIS completely disappear and heal up

Note: Acute exacerbation in Tr. II and Tr. III are expressed as Tr. II′ and Tr. III′.

fication by Kunitomo seems to be both clinically and scientifically quite satisfactory. In Japan, there is a debate at present on whether the onset of trachoma is chronic or acute. The late Prof. Yasushi Nakamura believed it is chronic, and Prof. Kunitomo and Dr. Y. Mitsui believe it is acute. I also hold the view that, regardless of the fact that most cases begin as a very low grade inflammation seeming nearly insidious and tend to be missed in the history, trachoma begins acutely. To understand the course and occurrence of trachoma in this fashion, Kunitomo's classification seems adequate.

One evidence of the progress that has been made since the congress of last year is that the use of electron microscope has become quite common. Dr. Yukihiko Mitsui of Kumamoto University (Kumamoto) in his study of Provazek bodies with the electron microscope has determined the location of the initial body during its growth cycle. According to his study the growth cycle of Provazek bodies goes through the eclipse period to the initial body then to the polygon and finally to the elementary body.

Dr. Waichiro Kamada, a disciple of Prof. Yasuharu Kuwahara (Tokyo Medical College, Tokyo) who is working on corneal transplantation of different species, reported that when a foreign cornea is soaked in the serum of the kind of the animal which will receive the transplanation, the cornea can be transplanted without reactive signs and that it can be sustained in its transparent or near transparent state. Kuwahara last year transplanted a chicken cornea on a human eye through the lamellar method with sufficient transparency sustained through one year's observation.

Prof. Tokuji Okuma (Yokohama University, Yokohama), who is a disciple of Prof. Shinobu Ishihara while continuing his work on improvement of Ishihara's test of color blindness and who published his own test in 1950, introduced another new test on this occasion. Gray spots of three grades of darkness are placed in a ring and one spot of red, green or purple is located in them. There are seven sheets to one color and each sheet has a different hue of color spot. The normal person can find all of the color spots in 21 tests, the incomplete color blind some of them, and the complete none. In this way the type and the degree of dischromatopsy can be classified and measured.

By examining 670 autopsy cases Dr. Shogo Hiwatari has shown that there is a very close relationship between arteriosclerosis of the central artery of the retina and brain hemorrhage.

An address by Prof. Samuel Kimura of the University of California on toxoplasmosis of the eye was received with great interest. Although this disease has not as yet been found in Japan it is expected that it will not be long before it is.

Seven addresses were presented on glaucoma and a heated discussion followed.

From Juntendo University two reports were given. Dr. Hirohiko Shibata *et al.* reported on 172 cases of excessive myopia of which the refractive stage was examined before and after lens extraction. It was substantiated that the refractive power of the lens increases proportionately to the refractive error and is an important factor in the etiology of myopia. By fixing the visual line of the healthy eye of strabismus patients on a movable target, Dr. Kazuo Kata was able to

measure the coordinate movement of the strabismus eye. By this method a transitional type between strabismus concomitans and strabismus incomitans was elucidated, and absolute strabismus concomitans was found to be comparatively rare.

There were many more topics of interest discussed at this Congress but to avoid a too lengthy discourse this report must be terminated here.

Note: There is one thing that must be brought to the attention of your readers. This is the matter of spelling of proper nouns. In Japan the names of places, schools and persons are written officially in character. Therefore there are times when a fixed English spelling was not established or known to the writer, and it was necessary to spell out these names in a manner which would be most easily pronounced by the reader. The spelling may happen to be different from the signatures of individuals concerned but this is inevitable.

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Clinical Practice

Accommodation and Refraction

TESTING OF VISUAL ACUITY IN PRESCHOOL CHILDREN: NORMS, VARIABLES AND A NEW PICTURE TEST

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Pediatrics, 1957, *19:* 1093–1100

Visual acuity in the human eye is not developed at birth; it develops during the early years of life, approaching the adult level by the age of 7 years.

The responsibility for determining the presence of normal vision in each eye of the preschool child rests with the physician in charge of the child's health. The physician may be either a pediatrician or a general practitioner of medicine. Examination of the eyes is an essential part of the general physical examination. As an amblyopic eye usually appears normal on objective examination, testing of visual acuity by subjective methods is necessary. Gunderson recommends that this be performed on or near the child's third birthday. Its prophylactic importance is fully comparable to that of routine immunizations as part of the preventive program for the individual child.

Most children 3 or 4 years old are unable to identify letters or numerals. Many youngsters 3 years of age and older with superior intelligence can be tested accurately with the illiterate E. However, there are always some children up to 5 years of age who are unable or unwilling to cooperate in this test and who therefore must be tested by other methods. Picture tests have offered the most successful approach to the problem, but most picture tests in current use have disadvantages.

VARIABLES IN TESTING VISION OF CHILDREN

Apart from amblyopia, refractive errors and organic disease, all of which it is the purpose of any test to detect, the most important variables which can influence the results of testing vision in children are as follows:

A. The child
   1. Physical condition
   2. Intellectual development
      a. Sense of form
      b. Span of attention
      c. Visual memory

3. Emotional response
   a. To examiner
   b. To environment of test
   c. To test itself
   d. To others present (parents, siblings, etc.)
4. Experience
   a. With objects pictured
   b. With prior tests

B. The examiner
1. Personality
   a. Liking for children
   b. Patience
2. Experience
   a. With children in general
   b. With test employed

C. The environment
1. Illumination
2. Distracting elements

D. The test
1. Sensitivity and selectivity
2. Ease of administration
3. Single targets *vs.* charts
4. Working distance
5. Subject matter
6. Uniformity of response

1. Sensitivity and selectivity. It is of no importance if a test does not distinguish between ametropia, amblyopia, or organic disease, since any one of these conditions is sufficient cause for referral to the ophthalmologist. A test which is sensitive to differences in acuity of the order of two will detect most disorders of clinical significance.

2. Ease of administration. To be useful on a large scale, a vision test for young children must be capable of being administered and interpreted by lay persons such as preschool teachers and volunteers.

3. Single targets vs. charts. We have noted that visual acuity is dependent upon the form sense and that this sense is imperfectly developed in young children. Ehlers states that the sense of form is most easily utilized in an otherwise empty field. Simultaneous exposure of several different pictures confuses and distracts the young child. Secondly, rapid memorization of shapes and locations of pictures on a chart may give falsely positive results on testing of the second eye. Both of these disadvantages are eliminated when individual pictures are used. Finally, it is doubtful whether any of the picture charts in common use in this country have been standardized on groups of children with normal or subnormal vision.

4. Working distance. Most 4-year-old children cooperate well in tests performed at 20 ft. Three-year-olds and others who lose contact with the examiner require

a test which varies the visual angle by distance instead of by target size; 15 ft. has proved a practical distance for these patients.

5. Subject matter. Test objects must be sufficiently numerous to minimize the probability of lucky guesses. Characters like the illiterate E offer a 1-in-4 chance of a right guess.

The main advantage of pictures over characters is that pictures can have greater reality and interest for a child. To have reality, they must represent objects within the familiar experience of children. Scarcely less important, they should evoke a pleasant, rather than an unpleasant, emotional response in the child's mind. Thirdly, they must provide diversity of subject matter for children of differing tastes.

Theoretically, drawings should not be distinguishable from other pictures in a series solely on the basis of outline. Since the importance of visual angles is paramount, careful attention must be paid to the proportion of black to white in the internal structure of a design. If several drawings of a single subject vary in respect to this proportion, surprising differences in the blur pattern result when the viewing eye is ametropic or is made so artificially. Under these circumstances, thin lines disappear entirely and those that are too thick appear as amorphous black blobs, especially at points of intersection. To convince oneself of this, one need only view some of the picture charts in current use with one's distant vision blurred by a weak convex lens.

Finally, the distance at which a given picture can be recognized by a normal child of a given age must be established by actual trial with children of the age group to be tested.

6. Uniformity of response. For reasons that have been indicated, it is highly unlikely that any individual child will show a narrow distribution of response levels for all test objects, or that any one object will be recognized at the same distance by all subjects. Provided that the probability of guesswork can be eliminated, a few correct answers have positive significance. Standardization of the test must be in terms of the least vision which will permit recognition of a test object at a given distance. To this end, values must be established for the maximum distance at which a target can be recognized by an eye with a known level of visual acuity.

A NEW TEST OF VISUAL ACUITY

With the preceding considerations in mind, a series of black-and-white pictures was designed (Fig. 1) which could be recognized with about the same facility as the letters on the 25- and 30-ft. lines of the Snellen chart. Much time was spent in viewing preliminary drawings through blurring lenses in an effort to produce pictures which would be recognizable at 20 ft. with acuity levels no lower than 20/25 or 20/30. Initial trials with preschool children resulted in the selection of eight pictures which seemed to have the highest interest value and the most consistent recognition levels for the group. The common denominator of all the pictures is that they represent objects within the experience of 3-year-old children. This fact, the construction of the drawings, and individual presentation

FIGURE 1. Preschool vision test and 30-ft. E (actual size). In the test itself the characters are printed on plastic as individual pages in a ring binder. (Courtesy of Allen, H. F.: Pediatrics, 1957, *19:* 1093, Charles C Thomas, Publisher.)

of the pictures are believed to represent improvements over picture charts in current use.

RESULTS

It was readily determined that each of the pictures could be recognized at 20 ft. by most normal 4-year-old children and at 15 ft. by most normal 3-year-olds. Some 4-year-olds could see certain pictures at distances slightly greater than 20 ft. just as some adults can recognize letters below the 20/20 line on the Snellen chart.

Older individuals with reduced acuity often showed a wide variation of responses to the different pictures. The pattern of this variation was seldom the same even among individuals with the same level of Snellen acuity. Correlation of the pictures with the 30-ft. illiterate E showed that the distances of maximum recognition were about the same for each. Vision of 20/30 (Snellen) gave results under 20 ft. for every picture but one. Vision of 15/30 (20/40 Snellen) did not

permit recognition of any of the pictures at 20 ft. Vision of 10/30 (20/60 Snellen) gave maximum recognition distances in the vicinity of 10 ft. Lower acuity levels corresponded with proportionately shorter recognition distances.

Comment: As a result of the considerable interest shown by regional, state and local associations for the blind in developing preschool vision screening clinics, the value of such programs, as well as some of the pitfalls, are becoming much more evident. Certainly an early recognition not only of vision defects, but also of other ocular conditions which are not apparent upon casual inspection, is most important for the visual future of the child.

While most ocular conditions which need attention may be revealed by defective vision there are others, however, where, even though vision with each eye is apparently undiminished, intraocular disease may be present, or where binocular vision presents difficulties. The most efficient type of ocular survey would be a thorough ophthalmologic examination, but this is, of course, impossible as a mass procedure. While there can be no adequate substitute for such an examination, a visual test combined with some tests of ocular function may be given satisfactorily by lay persons who have had some small measure of training in the technique of examination. At the present time in a number of cities several hundred volunteers, composed mostly of Parent-Teacher Association mothers and members of medical society auxiliaries, Junior League, and other civic groups, are conducting screening programs among 3- to 5-year olds, apparently with considerable success. In other communities this work has been carried on by the county associations for the blind, and in areas where there are kindergartens the school or public health nurse is entrusted with the program.

There is no question but that these volunteer screening groups will increase and may soon be a familiar entity in each area. In many cases, however, they are set up without the active supervision or advice of an ophthalmologist, and in such cases there is, of course, some danger of their being used by those nonmedical individuals who are primarily interested in supplying glasses. It should also be recognized that any visual deficiency found in such tests is not necessarily indicative of a correctable refractive error but may represent the effect upon vision of intraocular disease, and it must be impressed upon those having to do with the screening programs that diagnoses in such cases can be made only by an ophthalmologist.

As to the methods of testing, those presented by the author of this paper, including the picture test which he has devised, seem most acceptable and fit in well with the experience of ophthalmologists in general. The older picture tests, as everyone who has had considerable experience with them will testify, are unsatisfactory. Whether it is advisable or not to recommend the Allen Picture Chart, properly called the "Preschool Vision Test," for surveys administered by nonmedical personnel remains to be seen. Certainly it would be well to experiment with it provided there is ophthalmologic supervision of the procedure.

Ocular surveys should be an integral part of every general physical examination of a child, regardless of the age. Every general practitioner or pediatrician should have and use in each case the illiterate E test, or the picture chart here suggested. Visual tests for children too young to give subjective responses may be made by observing the child's behavior upon rolling small balls, such as different sized ball-bearings, and noting with what precision the child can coordinate hand and eye in reaching for them. However, it usually suffices to explore visual acuity only in those over 3 years of age unless there is some difficulty with the fixation of test lights or other evidence of ocular abnormalities.

Certain functional tests should be combined with the visual test when given by physicians or possibly even when given by trained lay volunteers. These should include observa-

tion of the ocular movements in order to see if both eyes move easily and fully laterally, medially and vertically. The presence of single binocular vision, sometimes absent even when each eye individually has good vision, may be determined by noting whether or not the child has controlled convergence as a light or small object approaches his eyes. In two of the tests which are now widely used for school children, anisometropia may be suspected although not definitely diagnosed if the child is able to retain visual acuity in one eye when +1.50 D. spherical lenses are placed before both eyes. This is a definitely helpful test, and, in my experience, can be used successfully in most of those within the 3- to 5-year age group. Use of the ophthalmoscope and adequate external ocular inspection is, of course, necessary and it is assumed will be part of any examination done by a physician.

Considering the whole problem in the light of the foregoing, therefore, it would seem to be desirable for ophthalmologists to encourage the ocular examination of preschool children, to take over the responsibility of training the volunteer workers, and to inform the other physicians who are concerned with such examinations as to suitable and effective technic. In addition, under proper supervision and with suitable training, some simple but all-important functional tests could be added.

EDWIN F. TAIT

AN APPARATUS FOR GRADING THE VISUAL ACUITY OF INFANTS ON THE BASIS OF OPTICOKINETIC NYSTAGMUS

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Opticokinetic nystagmus is the nystagmus which is elicited by objects passing in succession through the visual field. Ophthalmologists and neurologists have employed this response in the analysis of hysterical blindness and as an aid in localizing certain intracranial abnormalities. However, its possibilities as a test for visual acuity in infancy have not been sufficiently explored.

In the study of opticokinetic nystagmus the authors first employed a kymograph drum covered with vertical stripes; this was rotated at various distances in front of the infant's eyes. The occurrence of the response was so inconsistent that the method was abandoned.

The apparatus finally devised consists of a strip of rolled white paper 16 ft. (4.9 m.) long and 9 in. (0.23 m.) wide. Across the width of the paper are printed black lines which are equidistant and of the same thickness as the intervening white spaces—the first 8 ft. (2.4 m.) with an 0.02-in. (0.05-cm.) pattern and the second 8 ft. (2.4 m.) with an 0.06-in. (0.15-cm.) pattern. The whole strip is rolled manually from one spool to another over two narrow Plexiglas arcs. With

TABLE 1
Graded Responses in Relation to Age

Age	No. of Infants	Excellent		Good		Fair		Negative	
		no.	%	no.	%	no.	%	no.	%
1 day	20	10	50	8	40	1	5	1	5
2 days	28	18	64	7	25	2	7	1	3½
3 days	17	9	53	5	29	1	6	2	12
4 days	20	8	40	5	25	4	20	3	15
5 days	15	7	47	6	40	2	13	0	
Totals	100	52		31		10		7	

the edges of the paper resting on these arcs a tentlike affair is formed under which the child is placed, lying on a small mattress. The distance from the child's eyes to any point on the arc is approximately 6 in. (15 cm.). Two 25-watt flood lights placed in back of the infant's head supply a fairly even illumination. The spools have a gear ratio which moves the paper along at approximately 0.9 ± 0.2 in. (2.3 ± 0.5 cm.) per sec. when the handle of the spool is turned as slowly as consistent with smooth rotation.

One hundred newborn infants ranging in age from 1 hr. and 20 min. to 5 days were tested. Responses were graded as excellent when they were elicited immediately or shortly after placing the infant in the apparatus or if the nystagmus was well sustained throughout the testing period. They were rated good if there were periods of well sustained nystagmus but interrupted by conditions which might be expected to interfere with response such as sleepiness, crying, flatulence or marked restlessness. They were rated as fair when the periods of nystagmus were short and intermittent without obvious reason. Negative responses were so designated when there was either no nystagmus at all or, if present, was so fleeting that it could not be attributed to the stimulus of passing lines.

In all there were 93 positive responses: 52 excellent, 31 good and 10 fair. Table 1 shows the breakdown of graded responses in relation to age.

Lack of response is not final proof of blindness but a positive response definitely indicates the presence of vision. Perception of the 0.06-in. pattern corresponds to a Snellen notation of 20/670. This index, however, may be found to be lower when the study is repeated using a full range of line patterns.

Comment: This is a most ingenious modification of a very important method of visual testing. In large institutions, where one is constantly asked to determine the presence or absence of vision in infants, such a modification should prove most fruitful and helpful. Devices used by the discussant to elicit the opticokinetic nystagmus in such cases has been limited to crude rotating drums with painted vertical stripes. We are most anxious to construct this apparatus, described by the writers, and urge others to do likewise, particularly in light of the reported high positive response rate.

HAROLD F. FALLS

CONTRIBUTION TO THE GENESIS OF AMETROPIAS BY THE STUDY OF UNIVITELLINE AND BIVITELLINE TWINS

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Arch. opht., 1957, *17:* 38–43

An attempt has been made by comparing ametropic twins to determine the respective influence of genetic factors on the one hand and of environmental factors on the other, in the genesis of disorders of ocular refraction. The univitelline or bivitelline character of the pairs of twins constituting the study material was established (1) by examination of the placental membranes, when possible; (2) by the characteristics of resemblance; and (3) by the determination of blood groups and factors according to the Penrose method. This last criterion alone usually establishes a probability of more than 80 per cent. The three criteria mentioned provide concordant indications, which made it possible to determine the univitelline or bivitelline character of all the twins studied with almost absolute certainty.

The study material consisted of 28 pairs of twins, half univitelline and half bivitelline. In 13 of the pairs in each group, the ametropia consisted of hypermetropia or hypermetropic astigmatism; and in the other two pairs it consisted of myopic astigmatism.

Tabulation of the findings showed that the hypermetropia and hypermetropic astigmatism of the corresponding eyes are almost identical in univitelline twins, but that they may differ more or less sharply in bivitelline twins. This finding, which agrees perfectly with those of earlier workers, warrants the conclusion that genetic factors play an essential part in the development of hypermetropia and astigmatism. The familial character of certain cases of strabismus and of certain cases of closed angle glaucoma can undoubtedly be attributed to this fact.

By contrast, the appearance and, even more, the progress of pronounced myopia seem to be determined by causes of unknown nature. In the pair of univitelline twins with myopia and astigmatism, the astigmatism was similar but the myopia varied greatly in degree. The pathogenic problem posed by this finding is as yet unsolved. The facts so far observed seem to lead to contradictory conclusions. Thus, in certain families many individuals are affected by high myopia, which argues for the importance of a genetic factor in the appearance and development of this ametropia. On the other hand, certain cases of myopia are not genetic in origin and can only be due to environmental factors. For example, eyes affected in early age by a long-lasting disease, such as phlyctenular keratitis, may eventually exhibit axial myopia that is severe and progressive.

It is quite possible that the dissimilar myopia of the twins referred to should be attributed to nongenetic factors. These univitelline twins were probably premature, and it has been shown that prematurity creates a predisposition to myopia. A third possibility that must be considered is that the predisposition to myopia is genetic in origin, but that the development of the condition varies according to the influence of unknown factors. In any case, it seems that identity of hypermetropia or astigmatism in two twins is an argument in favor of univitellinity, but that an inequality of high myopia in two twins does not justify excluding the possibility that they are univitelline.

Comment: The problem of genetic influence in errors of refraction continues to remain most complex and unyielding. Apparently no easy answer is forthcoming.

It has been repeatedly emphasized that it is erroneous to attempt to ascertain genetic influence in errors of refraction by simply taking into account the total clinical refraction. This total clinical refraction of the eye is apparently the product of a combination of several variables, each of which may be independent in its hereditary transmission. Such variables include the following: (1) depth of the anterior chamber, (2) axial length, (3) lens refraction, (4) corneal curvatures, and (5) question of master gene influence toward securing emmetropia.

In an extensive twin study, conducted by Dr. Waardenburg, pertaining to errors of refraction in twins a considerable range of variability in the error of refraction in hyperopic uniovular twins was found to exist. The range was up to 2.75 D. In his uniovular myopic twins an even greater degree of variation was found even though very high degrees of myopia were excluded. An even greater difference in variation between both the hyperopic and myopic binovular twins was demonstrated. Dr. Waardenburg's study supported the contention that genetic influences played a considerable role in the determination of errors of refraction and that this hereditary influence became more conspicuous with the passage of time. The reverse situation developed in the case of binovular twin follow-up studies.

Dr. Weekers and his associates have carefully pointed out the criteria for determination of the binovular and uniovular twins: (1) Extensive and careful serology, (2) cord data, and (3) superficial similarities.

Even with such careful analyses as the above it is difficult at times to be certain of the identity of the twins. This point should always be kept carefully in mind when reading the report of twin studies. In Dr. Weekers' pair of myopic uniovular twins the influence of environment (prematurity) cannot be excluded. Furthermore his conclusions must be carefully weighed, particularly in light of the limited number of twin pairs, the lack of any evaluation of the influence of time (short term study), and insufficient knowledge of the state of maternal health, length of pregnancy, and so forth.

There is a great need for an extensive and very long term twin study devoted to a careful analysis of the development of all the various components of the total refraction from birth to adulthood. Many of the larger clinics in the country could support and expedite such a carefully controlled study with profit both to genetics and ophthalmology.

HAROLD F. FALLS

RETINOPATHY OF PREMATURITY (RETROLENTAL FIBROPLASIA) IN CHILDREN IN WHOM THE DISEASE HAS NOT PROGRESSED TO COMPLETE BLINDNESS, AND THE SUBSEQUENT INVESTIGATION OF CASES OF MYOPIA

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Brit. J. Ophth., 1957, *41:* 321–337

This study concerns the examination of 30 children known to have had retrolental fibroplasia in infancy but in whom some degree of vision could be expected. In 85 per cent of the cases myopia varying between 2.5 and 18 D. was found.

Where the two eyes were equally affected by the retinopathy of prematurity, it was the eye with the better vision which showed the myopia, and where retinoscopy was possible in the more severely affected eye, a hypermetropic or emmetropic refraction was found.

The corrected visual acuity did not exceed 6/12 even in those cases with the least fundus changes. Where it has been possible to follow up these cases, the evidence suggests that, in the great majority, the myopia has not progressed. One of the exceptions to this was one of triplets, who showed an increase in myopia of the order of −3 and −4 D. in the right and left eyes respectively over a period of six years, while her triplet sister showed virtually no change in the same period.

Nystagmus was present in half the cases with useful vision. In the majority, the movement was fine and somewhat variable in rhythm, and its direction horizontal, vertical, or rotatory; frequently the different movements were present in the same eye at different times. Eccentric fixation was associated with the nystagmus in five cases.

Fourteen showed unilateral microphthalmos. The microphthalmic eye usually possessed little vision and frequently showed a convergent squint.

Seventeen cases in the series showed strabismus; 16 of these were convergent squints, and one also showed vertical imbalance due to a secondary overaction of the inferior oblique. The other case showed a latent vertical heterophoria. Usually, the strabismus was secondary to the eye disease which had led to gross visual impairment of the squinting eye.

Opacities in the ocular media were frequently encountered. Three grossly damaged eyes showed corneal opacities, and one case presented lenticular opacities. Vitreous opacities were evident in two thirds of the cases.

Malformations of the optic nerve head were noted in 14 cases. The appearance in some cases was that of a coloboma of the disk, while in others the disk appeared to be distorted as the result of contracture of scar tissue. Remnants of glial tissue were seen at the nerve head. Distortion of the nerve head was sug-

gested by the tortuous course of the retinal blood vessels as they emerged from the disk.

Thinning, atrophy and depigmentation of the retina were commonly encountered. Large areas of scarring with pigment disturbance were seen in many fundi where the disease process had been moderately severe; in the most minimal cases, a fine pigmentary mottling of the "pepper and salt" variety was apparent at the periphery of the fundi. A "bone corpuscle" type of pigmentation was also noted in some of these cases.

The macula in certain cases appeared elevated and slate grey in color, while in others it looked red and granular. A fine strippling of pigment was evident in many cases.

The retinal vessels sometimes showed an increased tortuosity, and a diminution in the caliber and number of branches was also noted.

Detachment was evident in 14 cases. In 13 of these the detachment was localized, the area most often involved being in the temporal half of the globe. Frequently the detachment was triangular in shape, with the apex of the triangle pointing towards the disk and the base in the region of the ciliary body. Two cases developed a retinal detachment at the age of 5 years, while in another a vitreous hemorrhage developed (which subsequently cleared up) at the same age. A third child, now 6 years old, has recently been reported as developing a retinal detachment.

Retinal folds were apparent in five cases, and in one case retinal folds extended downwards and laterally from the disk in both eyes, the symmetrical, bilateral appearance suggesting a genetically determined lesion.

The myopic refractive error occurred in such a high proportion of these cases that, although the series is small, there is ground for suggesting that the association is a real one. The precise nature of the connection between the two is by no means clear; myopia does not appear to occur in the eyes which are severely affected, and, as has been previously mentioned, where the two eyes are unequally affected it is the eye with useful vision which shows the myopia. It is possible that the myopia develops through the weakening of the globe by disease, but this hypothesis does not explain the finding of a hypermetropic refraction in the more severely affected eye. This latter finding may be analogous to the unilateral microphthalmos which may occur in rubella with uniocular lens changes.

The noxious effect of the rubella virus on the developing eye occurs in the first three months of pregnancy, and the effect of prematurity on the eye takes place in the neonatal period, yet there appears to be some fundamental resemblance between the two in their effect on ocular development in that both cases may represent an arrest of development.

Clinically, the findings in these myopes bear resemblances to other clinical types already described in textbooks as congenital axial myopia. In most cases, the diagnosis of congenital myopia is not made until the second or third year of life. The commonest clinical picture described in the cases of congenital myopia recorded hitherto is that of "partial albinism," where the interior of the

eye is lacking in pigment. It is postulated that, in this condition, the inner eye alone is affected, the remainder of the body being normally pigmented.

In view of the finding that retinopathy of prematurity is associated with myopia, and that in certain cases it has been possible to correlate myopia with prematurity, it is suggested that the association between the two is a real one, and that prematurity is one of the factors in the causation of myopia.

Comment: From time to time every ophthalmologist who sees any considerable number of children will encounter a child who seems to be myopic to an extent which would suggest that the condition was present at birth, but probably only in a very few of these cases is inquiry made regarding the possibility of prematurity. As a result of the limited information which many ophthalmologists have obtained by such inquiry, and also as the result of the routine ocular examination of premature infants which was carried on in most hospitals during the period when retrolental fibroplasia was common, many of us have noted, on the basis of the ophthalmoscopic lens needed to see the fundus, that many of these children were myopic and thus differed from the great majority of full term babies who were, by and large, hyperopic.

Because of the present day preventative measures as far as retrolental fibroplasia is concerned, it is doubtful that any further series of such cases can be assembled for study. There will, however, be plenty of prematures and the paper now being considered will undoubtedly stimulate further interest in the cause of refractive errors, particularly myopia.

From the practical clinical viewpoint, myopia, either congenital or developing during the first few years of life, would not be a matter of great concern except that it could be the prelude to a progressive or malignant myopia which would ultimately produce an ocular catastrophe.

Summarizing and interpreting the available reports on the subject, it would seem that fundamentally there are two types of myopia: one in which the condition is purely physiologic and a result of the normal growth processes, and the other the rather rare type which may be called "progressive" or "malignant" myopia.

Occasionally also encountered in a newborn with a rather high degree of myopia, who maintains about the same amount of myopia throughout life and is therefore not a "progressive" myope. The usual child, however, is hyperopic at birth, becomes less hyperopic as time passes, and eventually may go through the emmetropic stage (except for astigmatism) to myopia. All of this ordinarily occurs without the development of any marked amount of ciliary hypertonus or of particular discomfort and the development is usually complete at the time of ocular maturity in the second decade of life. Such normal development follows the usual pattern of growth in that it is not constant but is in the form of periods of fairly rapid growth punctuated by periods of no change. In such normal cases, the progress towards myopia, however, rarely exceeds 0.75 D. per year, and if the change is 0.50 D. or less for several consecutive years, the whole thing may be considered as physiologic and a lens correction will simply restore the normal accommodative and convergence requirements and provide normal vision for both distance and near fixation.

In the second type of case, that involving a malignant type of myopic development, the myopia is apt to be present at birth or to develop during the first few years of life; the amount of development will ordinarily exceed 0.75 D. when averaged over a period of several years and will not stop early in the second decade, but may continue into the fourth and even the fifth decades.

All available evidence seems to indicate that physiologic myopia is simply an expression

of the normal growth of ocular structures producing an anatomic situation in which the focal length of the optical system of the eye does not quite coincide with its physical length. As an anatomic peculiarity, this type is in the same class as big feet or small feet, or a long nose or a short one. As a rule, normal accommodative amplitudes accompany the physiologic type of myopia, especially if the patient has been wearing corrective lenses.

Many ophthalmologists, including this reviewer, have had considerable experience over many years with both types of myopia and are well aware of the fact that nothing which the patient may or may not do in the form of exercise will have any effect upon the basic refractive error.

Malignant myopia presents, clinically, quite another problem. When a child manifests a very early development of myopia and shows with his second or third yearly examination an increase which is more than would be expected with a purely physiologic development, it is time to consider what might be done to prevent a further abnormal increase. Clinical studies over a number of years reveal many cases whose developmental curves have apparently been inhibited by attention to general health factors and possibly by the use of bifocals. The first measure is obvious, but there is still considerable question as to the role of bifocals in such cases.

Bifocals, of course, do not help as far as vision is concerned, but they do make unnecessary the use of normal amounts of accommodation, and the latter may possibly be a factor in the increase of myopia. Ample clinical experience has shown that bifocals do no harm in such cases. There is no positive evidence of any inhibitory action of bifocals in the child with an apparent progressive myopia, and of course there is no possibility of effective experimentation in the matter. Clinical evidence, however, suggests that there may be something to the idea that normal accommodative efforts, such as would be required with a full lens correction, may be a causal or at least accessory factor in the production of increased myopia, although the mechanism by which this is accomplished has not yet been described acceptably.

EDWIN F. TAIT

THE SURGEON'S VISION

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Nature sometimes plays a "dirty trick" on a surgeon because, by the time he becomes successful and acquires a reputation he may also have reached the age of presbyopia. No matter what type of visual aids are used in presbyopia they are but imperfect substitutes for the great facility of accommodation of youth. And even though expert advice is readily available to the surgeon he is frequently so busy that often he does not avail himself of certain types of glasses which would be of great help in his work. Many surgeons use only one pair of

glasses for all tasks, but all surgeons should be familiar with the more common types of lenses and magnifiers. Almost everyone is aware that as the bifocal segment reaches the average maximum strength the range of near vision is only about 4 in. This creates a blurred area in the intermediate, or arm's length, distance. In this situation a device which is not generally known may be of great help. It consists of bifocals in which the upper portion of the lens is ground for intermediate distance and the lower for near. Although such a pair of "occupational bifocals" cannot be used to see distance, they are of great advantage when surgery is performed in which the field consists of near and intermediate vision.

If it is essential to see distant objects while maintaining both near and intermediate vision, then some form of trifocal lens is indicated. A variety of styles is available and they may also be fitted at various heights to the eyes so that the very first pair may not always be the most satisfactory. A double bifocal lens, in which the upper segment is made for any desired distance, is very useful for gynecologic examinations and procedures, or to see the throat or ear drums. It can also be applied in such a manner that the central section is used for intermediate and the upper segment for distance (a "minus add").

Another way of aiding accommodation is by means of clip-on lenses. These can be ground to clear the near vision or any near or intermediate distance but have the twofold disadvantage of blurring the distance vision and of being limited in range when the power reaches a certain point.

If the magnification obtained by means of glasses is insufficient one must resort to some sort of loupe. Many different forms of loupes are available, but generally speaking they fall into two categories. The first type consists of strong magnifying lenses combined with prisms which are held a few inches before the eyes. The following are examples of this type of arrangement:

1. The Beebe loupe consists of partial eye glass rims with temples and can be worn with or without glasses. The magnification is about two times and the range at which an object is seen is from 8 to 9 in.

2. The B. & L. Dua-loupe is similar to the Beebe loupe, but it has a hinge on the frames so that the magnifying lenses can be folded up and out of the way. Its viewing range is 6 in. and it magnifies about three times, and an illuminator may be attached to it.

3. The May loupe is similar to the Dua-loupe and besides having the hinge it can also be unhooked from the frames. Its latest modification consists of only the holder for the magnifying lenses which can be hooked onto almost any ordinary glasses. These loupes come in four strengths giving a range of either 4, 7, 10 or 12 in.

The other category of magnifying systems consists of miniature telescopes such as the Zeiss spectacle magnifiers. These magnify about two times and the viewing range is about 8 in. The obvious advantage is the absence of a protruding device which holds the magnifying lenses. The Zeiss magnifiers come either plain or with attachable rims for single vision or bifocal lenses. Present Zeiss magnifiers are made in the Eastern Zone of Germany and the new type in the Western Zone is not as yet available.

The Cameron loupe is similar to the Zeiss. It also magnifies about two times and is available in two ranges, namely 8 to 10 in. or 12 to 14 in.

The Keeler magnifying spectacles consist of plastic frames which are fitted to the wearer, a bridge with the appropriate pupillary distance, and the telescopic units which are screwed into it. This forms a permanent arrangement for the surgeon and the shape of the frames permits ventilation under the eyebrow. The reading addition, if any, is ground into the lenses in the frames. Their disadvantage is that no provision is made for distance correction for those who need it, but its advantages are many. Its magnification is two times at a range of 10 in.

Comment: Onset of presbyopia always requires an ophthalmologist to consider the use of one of the available types of magnifying appliances so that he may be able to do an adequate inspection of the external eye and also obtain a helpful magnification of the ocular structures during ophthalmic surgery. Indeed, most ophthalmologists, regardless of age, use one or more of the various types of magnifying devices in their work. Frequently, however, the general surgeon, or the specialist in other types of surgery, will be working in an adjoining operating room with a pair of glasses totally inadequate for his visual requirements. In most cases the ophthalmologist would contribute greatly to the comfort and efficiency of his confrere if he would suggest that a study be made of the latter's visual requirements and that lenses be designed to meet them.

As a rule, it is not possible for the ophthalmologist to prescribe suitable operating glasses for a fellow surgeon as a result of data obtained only in the office, especially in the case of individuals 50 years of age or older. For proper results, it is necessary to observe the surgeon while he is at work, recording exactly the distance of his eyes from the operative site and noting the most comfortable position for his head. When these facts are known, it is then possible to design suitable lenses, utilizing either single vision lenses, bifocals, or trifocals or, if necessary, telescopes. Regardless of the accuracy of the lens prescription, however, none of these devices will be efficient and comfortable unless they are mounted in a properly fitting frame. While, as a rule, the dispensing optician can be relied upon to provide the latter, he is seldom able to design the lenses correctly because he has no way of being familiar with the actual requirements of the user.

These observations, as far as the ophthalmologist is concerned, apply not only to surgeons but also to a considerable number of the ophthalmologist's other patients. Many individuals who have been properly refracted may be uncomfortable in their occupations simply because the proper type of multifocal lenses have not been designed and fitted. In these cases the specification of lens type, form and position is the duty of the ophthalmologist and should not be left to the optician who dispenses the glasses.

EDWIN F. TAIT

The Lens

CONTRIBUTION TO CONGENITAL CATARACT

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Detection of congenital cataract in a young patient still presents a difficult problem when the child cannot see as much as would be necessary for a normal and harmonic development. Many questions concerning the cause of opacity of the lens, its form, its accompanying ocular symptoms and those of the entire body remain to be answered. An attempt is made to discuss briefly some of the questions, but the experiences of a single ophthalmologist, and even of one clinic, are insufficient in order to make progress. The author hopes that his paper may form the basis for an exchange of opinions among clinicians about congenital cataract.

Of 89 patients admitted to the ophthalmologic clinic of the University of Zürich and to the Policlinic of Zürich between 1945 and 1955, a causative factor could be found with more or less probability in 23 patients, 10 of whom had a definitely hereditary type of congenital cataract. In the case of 3 patients the mother had had German measles (rubeola) in the course of the first months of pregnancy. In 8 patients the mother had a chronic disease during the entire pregnancy or an acute disease at the beginning of pregnancy (severe sore throat in 1, fever and colibacillosis in 1, acute nephropathy at the beginning of pregnancy in 2, atrophic kidney in 1, unexplained febrile disease in 2, toxoplasmosis in 1). One infant had uveitis at birth and 1 fetus was injured by roentgen irradiation of the mother between the third and seventh weeks of pregnancy. In the remaining 66 patients, i.e., in almost 75 per cent of the total number of patients, it was not possible to determine the cause of the congenital defect. It will be necessary to record the history more carefully and to subject the parents to a thorough examination in order to get more information concerning the cause.

The main problem is what to tell the parents. There are several definite points which may be taken into consideration for the evaluation of a case: (1) Clarification of an occasional cause (hereditary factors, embryopathy). (2) Differentiation between the various forms of congenital cataract (unilateral or bilateral, partial or complete, stationary or with a progressive course). (3) Concerning the bulbus as a unit, distinction between otherwise normal eyes and those with accompanying abnormal symptoms. This is of great importance; these symptoms may be structural, trophic, inflammatory, of motor or functional nature. The severity and variety of the disturbances of this group play an im-

portant part in the operative and functional prognosis of the individual patient. In the series reported, nystagmus played the main part in about 33 per cent of the cases, strabismus in another 33 per cent and marked microphthalmia in 25 per cent. Changes in the fundus in the sense of an embryopathologic chorioretinitis were found in 10 per cent. (4) Consideration of the general accompanying symptoms in addition to the ocular abnormalities. The general abnormal condition of children with congenital cataract is of great importance, and general lesions play an unfavorable part with respect to the operative and functional prognosis. There was a high incidence of general delay in the development and of disturbances of the brain stem. Cardiac defects played a minor part.

These four points of a diagnostic nature and their significance for prognosis have been accepted in modern literature. The author believes that ophthalmologists should consult with pediatricians and biologists who devote themselves to hereditary problems in order to elucidate the physiopathology of the cases of these impaired and often underdeveloped children in an effort to devise a more basic treatment. This is a task which is of importance with regard to prevention of blindness.

Agreement has not yet been reached with respect to therapy, the age of choice for the operation and the surgical procedure. The least traumatic operative method should be employed. There is some agreement that one should operate upon eyes with less than 0.4 visual acuity. This general precaution shows that complications are severe and frequent.

This short paper does not permit a detailed discussion of the advantages and disadvantages of the various methods. But one exception will be made and that with respect to optical iridectomy and to Franceschetti's coreopraxy because these methods have been considered as antiquated, particularly by American workers. Surgical intervention on the iris is indicated in cases of a central, nonprogressive opacity. It is possible that the cosmetic and purely optic results are less satisfactory than those of successful intervention on the lens. But the intervention is harmless, makes accommodation possible and requires the slightest optical correction. If the opacity should progress, it will still be possible to make use of additional methods. These are well known and among them should be mentioned the discussion of swelling which unfortunately may have to be repeated several times, linear extraction with or without iridectomy after discission or tearing off of the anterior capsule. The lens mass aspiration is used in cataracts with a fluid mass. Extra capsular and particularly intracapsular cataract extraction are usually employed in adults with congenital cataracts.

In the series of patients reported, optical iridectomy or coreopraxy was employed most frequently by Amsler. Linear extraction and capsulotomy were associated with a greater percentage of complications than the disissions. Optical iridectomy proved to be completely harmless.

The number of postoperative complications is great and the complications are severe according to reports in the literature. Secondary cataract, secondary dystrophy of the cornea, phthisis of microbulbus, severe hypertension and de-

tachment of the retina present an unfavorable prognosis. In one of the author's patients a bilateral detachment of the retina occurred 45 years after the discission. The surgical procedure should be of the least traumatic type.

It is not easy to determine the right time for the operation. On one hand, one would like to operate early to take advantage of the necessary optical conditions before the occurrence of nystagmus and in order to secure a satisfactory development of the child. On the other hand, one would prefer expectant treatment because the underdeveloped eye may recover occasionally. It seems that the eye tolerates intraocular intervention better when it is performed later in life. Surgical intervention is definitely contraindicated before the third month, because a physiologic intraocular hypertension seems to exist at this time (Dolcet). Monocular cataracts may be operated upon only between the ages of 4 and 12 years and even then without great hopes, because of the severe amblyopia which may be present in most of these eyes. Partial opacities which make fixation possible are usually operated upon shortly before the patient reaches the school age.

There is a disagreement with regard to the surgical treatment of complete bilateral cataract and of eyes with partial central opacities. According to Owens and Hughes, and Bagley the results are better if the eyes are operated upon after 2½ years and 4 years, respectively, than if operation is performed earlier. The author did not find any significant difference in the number of complications associated with either early or late surgical intervention; but he emphasizes the fact that pathologic accompanying symptoms were observed by the American authors in 33 or 25 per cent of the eyes operated upon, while such symptoms were observed in 75 per cent of the eyes operated upon by the author. In general, the initial condition in patients who are operated early is less favorable than in those who are operated late. Only blind eyes are operated early, but usually one may wait longer if the child is able to fixate an object. If one operates upon one eye only, one should select the eye which is most abnormal and delay operation of the better eye. Statistics concerned with the number of eyes operated upon are interesting, but additional statistics with regard to the visual function of the individual patient are also necessary. Only statistics of the latter type provide information with regard to the social part played by congenital cataract.

Only 25 per cent of the eyes in the author's statistics are able to read 4/10 or more, but about 50 per cent of the patients may reach this visual acuity. Fifty per cent of the eyes in the author's statistics have severe amblyopia or are blind; only one sixth of the patients are usually classified in this category. Although many tables have been prepared by the author they are not given in the paper because he considers them to be of only relative value.

The following conclusions are drawn: Every operation for congenital cataract has its advantages and disadvantages, and complications may occur quite late.

In underdeveloped children who have suffered an embryopathy, it may be advisable if one wants to operate to take the stage of development in consideration rather than the age of the child; this is true particularly when one has to deal with small eyes (as is frequently the case) which have a very slow development. In the same group of patients with abnormal accompanying symptoms both

eyes should be operated upon at a greater interval, because the risk of complications is high. To obtain binocular vision seems to be of secondary importance in such cases. The author is convinced that better knowledge of the local physiopathology of the underdeveloped and impaired eyes and of that in embryopathic children should be obtained first, before definite progress can be achieved.

Comment: Dr. Verrey's request for meticulous inquiry by the ophthalmologist into the state of maternal health, maternal exposure to exanthemata, prematurity, the rhesus factor and hereditary history as necessary steps to the establishment of the causative factor of congenital cataract is most timely. The ophthalmologist is urged to take the time to examine the lens and eyes of the parents or other available relatives, for such may exhibit similar or minimally modified lenticular changes sufficient to reveal the role of the gene as a causative agent. The author's insistence upon a meticulous ophthalmologic examination, complete physical examination and instigation of clinical studies designed to establish systemic causation is also commendable. Actually all such steps should be the routine procedure in such cases by a well trained ophthalmologist, and when one carefully analyzes the paper a sense of regret develops within the mind of the discussant that such are necessary every now and then to "jack up our awareness and completeness."

It is perhaps pertinent to list a number of constitutional diseases which have associated cataracts: galactosemia, Rothmund's syndrome, neurodermatitis, oculorenal syndrome (cataract, hydrophthalmos, renal tubule dysfunction), mongolism, incontinentia pigmenti and Sjögren's syndrome (ataxia, mental deficiency, dwarfism).

Noxious intrauterine agents responsible for congenital cataract include: rubella, toxoplasmosis, virus infections (measles, mumps, chickenpox, polio) and Rh factor.

The blunt fact concerning instigation of surgical interference in congenital cataracts is that surgery should not be undertaken unless the ophthalmologist is quite certain the patient will be benefited visually. The marked incidence of serious complications both ocularly and physically is common knowledge and should serve to deter surgery at least until the child is beyond 18 months of age, with the exception, of course, of those individuals with bilateral complete cataracts. In those children, however, capable of getting about and with only central lenticular opacities, a trial of school should be given before seriously considering surgical interference. In my experience the older the child the fewer the surgical complications. Both the eye and general constitution are "poor protoplasm" in many of the children with congenital cataract and frequently react badly to surgery and anesthetic respectively.

In our hands "optical iridectomy" has been of little value, perhaps due to the fact that the iridectomy permits utilization of the optically poorer peripheral portion of the cornea and seldom improved visual acuity to a useful degree. The procedure, as pointed out by Dr. Verrey, is quite safe.

Papers such as this one by Dr. Verrey, which urge consideration of the individual as a whole, establishment of etiology, conservatism in prognosis, and conservatism in instigation of a surgical procedure which frequently may be more harmful than helpful, are always welcome additions to our literature.

HAROLD F. FALLS

DIAMOX TO PREVENT HYPHEMA AFTER CATARACT EXTRACTION: A NEGATIVE REPORT

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Wound reopening and hemorrhage into the anterior chamber and sometimes into the vitreous continues to be one of the most distressing complications that can occur in an otherwise smooth convalescence after cataract extraction. Fortunately, in most cases the blood slowly absorbs and the visual result in the end is apt to be very good. In other cases, however, various complications that are the direct result of the accident (such as iritis, blood-staining of the anterior hyaloid and sometimes also of the cornea, secondary glaucoma due to blockage of the filtration angle, and prolapse of the iris) may appear.

Conclusions reached by the author in 1941 in a study of hyphema that occurred in about 7 per cent of 1,185 cases of cataract extraction have since largely been supported by the findings of others in several large series of cataract operations. These authors agree that the hemorrhage comes from the wound in most cases, and between the third and the sixth days. The age and sex of the patient, the state of the weather, the blood pressure, blood clotting mechanism, vitamin C deficiency, focal infection, syphilis, diabetes unless uncontrolled or severe, the type of the operation, and the use of adrenalin have no bearing on the problem. Good suturing of the wound is probably an important factor in prevention. Iridectomy may play a slight role. Loss of vitreous is significant. A deep corneoscleral incision with conjunctival flap is probably followed by a higher incidence of hyphema than is a more purely corneal incision. Trauma is very important, whether it occurs outside of the dressing, as from a bump or a blow, or whether it occurs beneath the dressing, as from tight closing of the lids or contraction of the extraocular muscles. Freedom of movement and the use of the fellow eye after the third day may be significant.

The "constitutional moment" that occurs between the third and the sixth days after operation deserves further investigation. A study of the healing processes and time table of an incised wound helps to show what is going on and is of great importance in providing a clue to the problem of the constitutional moment. G.B. Kara concludes a valuable report on the histologic appearance of a human eye four days after cataract extraction with the following remarks: (1) wound healing at the limbus began by fibrovascular proliferation and anterior epithelialization; (2) epithelialization and inflammatory reaction occurred around chromic absorbable surgical sutures, (3) despite the use of appositional sutures, there was posterior gaping of the wound; (4) there was evidence of considerable trauma, namely, detachment of Descemet's membrane and hemor-

rhage atound the major circle of the iris; and (5) necrosis of the sclera was produced by the suture.

From this report and the experimental work on ocular wound healing in the case of a conjunctival flap reported in the literature, it appears that the third to the seventh day is the time when the fibrovascular plug from the surrounding episclera begins to soften or change as the proliferation of newly formed blood vessels and fibroblastic activity increase. The stage is then set for the wound to give way, particularly when there is posterior wound gaping, and to tear across the new blood vessels and so lead to hemorrhage into the anterior chamber.

A second active factor in the production of wound rupture is the compression of the eyeball by the orbicularis, the external ocular muscles, and in some cases external violent forces that raise the intraocular pressure to a point at which the wound gives way. Some compression of the eyeball by the orbicularis and the external ocular muscles undoubtedly goes on daily from the time of the operation. Before the third postoperative day, such external compression may and probably does open the wound a little from time to time, but no hyphema occurs because the new vessel development has usually not progressed as yet to any great extent. When the proliferation of the new vessels is completed, the constitutional moment appears.

Even so, however, the constitutional moment does not yet seem to be satisfactorily explained. In 1933 and again in 1941, the author advanced the theory that this moment occurs when the intraocular pressure begins to come back to normal or even temporarily to be higher than normal as the formation of aqueous, partly depressed by the operation, begins to resume its activity and also when the wound, which might be leaking slightly up to that time, closes over completely. The increase in the intraocular pressure might stretch the healing wound, causing discomfort to the patient who would then voluntarily or involuntarily squeeze his eye by contracting the orbicularis, with wound reopening and hyphema as the result. Various studies have since been made of the intraocular tension in eyes subjected to cataract operations. Much more work, however, must be done on this subject, because as yet very little is actually known about it. The theory that in cases of hyphema the constitutional moment depends on the postoperative variation in pressure, if it does exist, associated with the diurnal phasic rhythm of the intraocular pressure and the concomitant variation in the episcleral venous pressure, is still attractive and may prove to be valid.

Since the carbonic anhydrase inhibitor Diamox (acetazoleamide) is widely used to inhibit the formation of aqueous in cases of increased intraocular pressure, an investigation was made to see what effect, if any, the use of this drug would have on the incidence of postoperative hyphema. A total of 100 consecutive patients were given 250 mg. of Diamox twice daily, beginning on the third postoperative day and continuing through the eighth day. Hyphema appeared in 24 of these patients. In two, obvious severe external force was responsible for the hyphema. In a control series of 120 consecutive cases of cataract extraction in which Diamox was not given, 17 per cent of the patients showed hyphema. Similar results were obtained by two other observers. From these three

series of cases, it can be concluded that Diamox has no effect in reducing the average incidence of hyphema after cataract extraction.

This, however, does not provide much help in a study of the constitutional moment. Since tonometric studies were not made in the cases in which Diamox was given, it is not known what effect, if any, Diamox would have on the daily ocular tension after cataract extraction. The problem is a difficult one, and its solution is not advanced at present by the reports of Thorpe and others that Diamox will hasten the restoration of an empty chamber after cataract extraction. This premise has not yet been completely accepted and in fact late loss of the anterior chamber has occurred in spite of the routine use of Diamox started before the emptying of the chamber appeared. The regulation of the intraocular pressure during convalescence from a cataract operation may be a factor in the appearance of the constitutional moment, but the problem is as yet unsolved. Attempts to solve it should include investigation of the influence of the rhythmic diurnal variation in intraocular pressure, the presence or absence of choroidal detachment and its time of disappearance when it is present in the first few days, changes in the epibulbar venous pressure, and the variation in the ocular tension of the fellow eye.

Comment: Dr. Vail has carefully analyzed the problem of intraocular hemorrhage following cataract extraction. Anterior chamber hemorrhages will continue to occur, although meticulous surgeons do accurate wound closures and use every reasonable method for preventing external pressure on the globe.

Diamox, by reducing the formation of intraocular fluids, will lower intraocular pressure in glaucomatous eyes and, to a lesser extent, in normal eyes. However, Diamox had no significant influence on the development of intraocular hemorrhage in Dr. Vail's series nor in Dr. Dunnington's. This ineffectiveness of Diamox, in regard to intraocular hemorrhage after cataract extraction, does not exclude the possibility that raised intraocular pressure at a critical moment is responsible for wound reopening and the associated hemorrhage. It may be that Diamox has very little effect on the intraocular fluid formation on the recently operated eye. Also, it has not been established that Diamox aids in the reformation of the anterior chamber or prevents the late collapse of the anterior chamber. Thus it is not established that Diamox has an important place in the routine postoperative care of cataract patients. There is some question as to whether Diamox should be employed in the presence of an existing hemorrhage. If the hemorrhagic material in the anterior chamber is removed largely by phagocytosis, Diamox may not interfere with the clearing of the chamber. If some of the blood in the anterior chamber is removed by virtue of flow from the posterior chamber into the anterior chamber and out the angle, then agents, such as Diamox, that reduce the formation of intraocular fluid and induce a rise in reresistance to outflow, may be undesirable to eyes with a normal intraocular pressure.

IRVING H. LEOPOLD

HYPOTONY FOLLOWING AN INTRAOCULAR SURGICAL PROCEDURE

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Hypotony often follows intraocular surgical operations, especially those performed for cataract or glaucoma. In most cases, no alarm need be felt because the normal intraocular pressure will eventually be reestablished without any permanent visual loss. In a few cases, however, complications may appear, particularly if the hypotony is accompanied by prolonged flattening of the anterior chamber.

Although opinions differ as to the exact mechanism by which it is produced, clinical and pathologic observations of eyes with postoperative hypotony suggest that, apart from loss of vitreous, reduced formation of aqueous is a prime cause of hypotony. A constant finding in eyes soon after intraocular surgical operations is edema of all of the intraocular tissues, as well as widespread hemorrhage. In contradiction to the report of Dellaporta, papilledema, which is discernible ophthalmoscopically, has not infrequently been observed in eyes with hypotony after operations for both cataract and glaucoma. On several occasions, also, the author has seen peripapillary retinal hemorrhages after extraction of cataract, although they too are said by Dellaporta not to occur. In one instance, considerable papilledema accompanied by hemorrhages was observed on completion of an operation for cataract extraction.

The symptoms of hypotony following an intraocular operation are primarily those of irritation. Lacrimation is frequent. The eyeball is injected, and this condition is often accompanied by edema of the eyelids. The corrected vision is always subnormal. The disappointingly reduced vision sometimes obtained from three to five weeks after cataract extraction may well be attributed to the fact that the intraocular pressure is still subnormal. Normally, the intraocular vascular pressure is adjusted to an intraocular pressure that is relatively constant and not too much lower than the intravascular pressure. The sudden loss of this intraocular pressure when the eye is opened apparently upsets this delicate balance, causing transudation of fluid, congestion, and hemorrhages. The choroidal detachment so often seen in eyes with postoperative hypotony is probably due to this transudation of fluid. The diminution of aqueous formation, which results for the most part from the edema, congestion, and hemorrhages within the ciliary body and the iris and which appears to be a major cause of postoperative hypotony, also seems to be largely responsible for prolonged flattening of the anterior chamber, especially when a demonstrable leak cannot be found and pupillary block is not present.

The possibility of pupillary block should be kept in mind in cases in which there is a shallow anterior chamber in a moderately inflamed eye after a round pupil cataract extraction. A posterior synechia is responsible for the pupillary block. The intraocular pressure is usually normal or above normal in spite of the shallow anterior chamber. An anterior synechia may form very quickly and will always result in secondary glaucoma unless the condition is recognized and corrected. A small needle knife opening through the iris will provide the necessary correction.

Adequate suturing of the wound is the best method of preventing postoperative hypotony. Three or more corneoscleral sutures should be used in cataract extraction. Postoperative injection of air is useful in determining whether the suturing of the wound is adequate. Additional sutures should be used if the air is not readily retained in the anterior chamber. Correction of hypotony after operation is required chiefly in eyes with flattened anterior chambers. Here again the injection of air is useful, because it raises the intraocular pressure to some extent and so permits a more rapid return to normal fluid balance within the eye. When the intraocular pressure is restored, the formation of aqueous may take place under more nearly normal conditions. Other things being equal, the flattening of the anterior chamber will then be overcome and the eye will regain its tone.

Hypotony caused by the loss of vitreous presents an entirely different problem and one that is not dealt with in this article.

Comment: There are many annoying complications of ophthalmic surgery. Of these, a truly soft eye can be more bothersome than a hard one. The title of this paper is somewhat misleading, since the author discusses at considerable length shallowing or absence of the anterior chamber. Though a leaking wound or a fistula will cause hypotony, the reviewer feels that the shallow chamber is due to the leak and not necessarily to the reduced intraocular pressure. The demonstration of a leaking wound is not easy and in some cases the accompanying choroidal detachment may be due to aqueous entering the subchoroidal space at the site of the incision.

The reviewer agrees that Diamox is of little value in restoring the anterior chamber. If hypotony is the cause of shallowing of the chamber, one might expect the condition to be aggravated by the use of Diamox. This has not been observed. Likewise, Diamox should not be used postoperatively in glaucoma surgery since, if aqueous formation is reduced, peripheral synechias or a less effective filtering cicatrix may result.

The hypotony following overeffective filtering procedures can be most annoying. It undoubtedly plays a role in the progression of lens opacities, the marked variation in the refractive error with blinking, and may even cause marked reduction in vision from wrinking of the cornea. This type of case requires surgical correction, since no drug is as yet available to increase the intraocular pressure.

P. Robb McDonald

CATARACT SURGERY

HAROLD RIDLEY

London, England

Ophth. ibero am., 1957, *19:* 89–97

The secret of successful cataract surgery lies in causing minimal distortion of the globe. The surgeon's fear is vitreous loss and, except in eyes abnormal because of subluxation of the lens and in some degenerate highly myopic eyes, the vitreous will not prolapse unless the globe is distorted by the surgeon or by restless muscle action of the patient.

So far as the general treatment of bilateral cataract is concerned, the best advice that can be given to those learning to operate can be summarized as follows: Use a Graefe knife to make a very large section of about 150 degrees at the limbus, cutting a wide conjunctival flap. Hold the knife lightly and keep it always in motion with a sawing action, moving the blade forwards as well as upwards. In intracapsular cases grasp the capsule as low down as possible and rock the lens sideways and upwards until the very last fragment of zonule has been torn. The golden rule is never to distort the eye more than absolutely necessary.

In cases in which only one eye is affected, or even when one eye retains reasonably good vision, simple cataract extraction leaves much to be desired. Aphakic vision is not natural and very often a patient seems to prefer to use an eye seeing only about 20/60 to an aphakic eye which with correction sees 20/15. A cataract spectacle lens of 10 to 12 D. placed some 15 mm. in front of the cornea magnifies the retinal image by approximately 30 per cent, which makes the sight of the two eyes incompatible because of aniseikonia. Furthermore, the best acuity is attained only when the view is through the middle of the lens, other directions causing distortion and prismatic displacement. Fusion of the images of an aphakic eye and an eye with a natural optical system is therefore impossible for a variety of reasons and every attempt to focus both eyes together leads to diplopia. If, however, the aphakic eye is left unfocused its image can usually be suppressed. A contact glass fitted to the aphakic eye sometimes restores binocular vision, but the 15 per cent magnification compared with the normal is usually more than the patient can tolerate. In addition, many cataract patients lack the dexterity to insert a contact lens, even though their conscious desire to regain binocular vision is sufficient to justify the trouble and irritation. Clearly the ideal solution is to restore the natural optics by an intraocular lens in the natural position. During the last eight years such a procedure has proved successful in a high proportion of cases. An artificial lens cannot, of course, change its curvature in accommodation, but in presbyopes the position differs little from the normal, since the senile lens has lost much of its elasticity. With the intraocular acrylic lens the depth of focus is often surprisingly good and since, with a fixed focus eye, slight myopia

is preferable to emmetropia, the patient can often read without a glass, which usually gives him great satisfaction.

The technic of the intraocular acrylic lens operation was fully described five years ago and is by now well known. A few important operative details, however, will bear repetition. The lens is made of Transpex I, the purest fully polymerized polymethyl methacrylate, which has a specific gravity of only 1.19, about half that of glass. Its weight is little more than that of the aqueous it displaces, so that it does not require very strong supports to maintain it in position within the eye. Provided the posterior lens capsule is intact, the muscular iris is quite able to maintain the lens upright and coaxial with the pupil. The small peripheral iridectomy normally performed as a "safety valve" for the aqueous passing from posterior to anterior chambers provides a useful window for observing the rim of the lens and it is reassuring to see the lens margin years later remaining just as it was set in place at the operation. An intact posterior capsule is quite essential to prevent downward dislocation and this, of course, necessitates extracapsular extraction of the cataract. The main disadvantage of leaving the posterior capsule in the eye is that it may thicken or wrinkle. If necessary, the membrane can be divided from behind by means of a knife passed through the pars plana. Luckily the presence of an acrylic lens keeps the capsule taut and free from folds in most cases.

The intraocular acrylic lens operation is really two operations in one and any error in surgical technic is apt to be unusually troublesome. If, however, all goes well so that the cataract is completely removed except for its intact posterior capsule and the acrylic lens is centrally placed behind a central and circular pupil, then a good result can be expected.

Convalescence is generally slower than with simple extraction, mainly because some degree of serous iritis is inevitable and the exudate, colored by iris pigment granules, settles on the front of the lens, which is not only a window but an important refracting surface. Provided the pupil is kept about half dilated, this exudate does not become organized and eventually clears completely. If, however, the pupil is allowed to contract, a pupillary membrane may form and may have to be divided. The procedure (corepraxia) is simple and the membrane, which is not adherent to the underlying lens, the surface of which is clean, can easily be cut.

Reexamination of all the patients who had intraocular acrylic lenses inserted at St. Thomas's Hospital in 1951, 1952 and 1953, with the exception of five in whom deliberate intracapsular extraction was used before it became known that this procedure was usually followed by late dislocation of the lens, clearly showed that the acrylic lens can be tolerated within the eye and give good optical results for five years at least. An aphakic cataract glass makes it possible to read an extra row of letters, but the intraocular acrylic lens gives much more natural sight and a better useful field of vision without peripheral distortion or apparent displacement of objects and without unnatural magnification. Its greatest advantage, however, is that after a cataract operation on one eye both eyes can be used simultaneously, restoring binocular vision.

Every operation has its complications. Those which experience has shown may follow the use of the intraocular acrylic lens consist of the postoperative serous iritis and late thickening of the posterior capsule that have already been mentioned, possible loss of the anterior chamber for some unknown reason, and late dislocation of the lens. Anterior displacement is rare in the absence of trauma, but occasionally the pupil may become irregular so that the lens rim is exposed. Stabilization, however, often occurs in these cases and the patients retain useful visual acuity. Posterior dislocation, which has occurred in about 6 per cent of cases, is a major catastrophe and is to be expected if the posterior capsule has been removed or seriously damaged at the operation. Clearly the lens cannot slide down the face of the vitreous if the posterior capsule and zonule are intact, and there is no evidence that these ever rupture spontaneously. Nothing can be done to remedy the displacement if it occurs, but fortunately the acrylic lens lying in the base of the vitreous seldom gives rise to inflammation and glaucoma as does the human lens, and the patient may still obtain good aphakic sight.

The new anterior chamber lens technic, devised to overcome these complications, has undoubtedly widened the scope of cataract surgery still further, but in monocular cataract the original acrylic lens design seems preferable because the intraocular lens is placed behind the iris where nature intended it to be. Plain extraction, with its simplicity, will always have a place in cataract surgery, especially for aged patients, but in years to come the use of intraocular lenses, which go far to solve the problem of monocular cataract, and the development of the new technic will, it is to be hoped, give cataract patients a nearer approach to the restoration of normal vision.

Comment: This is an honest appraisal of the acrylic lens operation by the pioneer in this field. Mr. Ridley has undoubtedly performed more of this type of surgery than any other ophthalmologist. The main advantage of it is the ability of patients with monocular cataracts to obtain binocular vision. This must be weighed with the disadvantages: a technically more difficult procedure than the standard cataract extraction, a fairly high incidence of postoperative iritis, and, probably most important, an incidence of posterior dislocation in 6 per cent of cases. These patients undoubtedly have the other, infrequent but annoying, complications of cataract surgery, i.e., secondary glaucoma and retinal detachment. It would appear to the reviewer that the treatment of any complications would be more difficult when an acrylic lens has been used.

Mr. Ridley deserves much credit for developing this procedure. It has stimulated a renewed interest in cataract surgery, especially in the development of acrylic anterior chamber lenses. The author's reports have always been factual and he has never been one to minimize his complications. This trait, unfortunately, is frequently lacking in authors of other new and radical procedures.

P. Robb McDonald

The Ocular Muscles

SEGMENTAL DEPIGMENTATION OF THE IRIS FOLLOWING MUSCLE TRANSPLANTATIONS

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Ophthalmologica, 1957, *133:* 231–236

Without entering into the technical details of all the various operations designed to correct paralysis of the rectus muscles, the authors discuss a singlular postoperative complication which consists of segmental depigmentation of the iris with a cellular reaction in the anterior chamber. Although this complication does not seem to be mentioned in the literature, they were struck by the frequency with which it occurs. Four patients, aged 41 to 49 years, were operated on for posttraumatic paralysis of the 6th nerve (affecting both eyes in one patient). The technic used consisted in anastomosing the lateral part of the vertical recti to the insertion of the rectus externus, which had previously been sectioned. The operation was completed by recessing the rectus internus. Nothing unusual was noticed during the immediate postoperative period, but after an interval of from 3 to 10 days a subacute iridocyclitis appeared. The results of the Tyndall test were positive and many cells were found in circulation. This uveal reaction lasted for from 8 to 30 days. The cells, which became pigmented fairly rapidly, were deposited on the corneal endothelium, especially in relation to the temporal part of the iris, which gradually lost its color. The pupil, even when no posterior synechias were present, became deformed, showing that the stroma was affected. In the patient with bilateral paralysis, the uveal reaction was extremely severe on the right side, on which he had had herpes ophthalmicus without visible ocular involvement some years earlier. Two of the patients—men aged 49 years—also presented fairly pronounced and definitive hypotonia of the globe.

When muscle transplantations are executed, the iris is deprived of the blood supply from the anterior ciliary arteries. The only nerve endings that are cut in disengaging the muscles, however, are the proprioceptive fibers for the muscle itself, and these endings therefore have no connection with the iris. It seems, then, that the segmental depigmentation and atrophy following transplantation procedures may be related to ischemia. Other forms of heterochromia (simple, cyclitic or of Fuchs, and neurogenic) are either hereditary or sympathetic in origin. The operative technic used by the authors does not in any way injure the vegetative fibers. Moreover, neurogenic depigmentation of the iris is entirely different in character from that observed in these patients.

Atrophic heterochromia, on the other hand, whether senile or secondary to

factors such as inflammation, trauma, glaucoma, ischemia, or myopia, is vascular in origin. Experiments and clinical observations have shown that ischemia of a determined retinouveal territory is followed by atrophy and changes in pigmentation in proportion to the severity of the circulatory deficit. Ischemia leads to sclerosis and hyalinization of the vessels and these in turn are followed by degeneration of the pigment cells. The chromatophore loses its dendrites, assumes a rounded shape, and discharges its pigment, which is deposited in the form of small granules on the surface of the iris and in the lower chamber angle. These changes were gonioscopically demonstrated in each of the patients.

The uveitis accompanying the loss of pigmentation was apparently catabolic and not infectious. Possibly the pigmentary disintegration dependent on ischemia was the underlying cause of the uveal reaction. The hypotonia of the globe might well be produced by an analogous mechanism (ciliary ischemia and atrophy). If this theory is accepted, it would be logical to try to prevent the depigmentation by assuring adequate irrigation of the iris by first transplanting the nasal half of the vertical recti and leaving the recessing of the rectus internus until later, to permit the development of a collateral circulation. In this connection, it may be remembered that Hartmann believes that not more than two rectus muscles should be operated on at one session.

SYMPOSIUM: ACCOMMODATIVE ESOTROPIA

Relationship between Accommodation and Convergence

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Classification and Diagnosis

Kenneth C. Swan

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Principles of Treatment

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Tr: Am. Acad. Ophth., 1957, *61:* 375–396

A rational approach to the therapy of accommodative esotropia must be based on a clear understanding of the mechanism underlying vergence movements and, in particular, of the roles of accommodative and fusional vergence.

Accommodative vergence may not develop fully until the child is about 2 years of age. The eyes must accommodate to see a near object of regard clearly, and they must converge to see it singly in binocular vision.

Nagel introduced the concept of the meter angle to define the vergence angle of the two eyes for any particular distance of an object of regard (Fig. 1). In essence, a 1-meter angle is the angle between the visual axes when a person binocularly fixes an object situated in the midline at a distance of 1 m. It is clear that the numerical value of a meter angle in degrees or diopters depends on the distance between the centers of rotation of the two eyes, i.e., on the interpupillary distance, as well as on the distance of the object of regard. The infant with his narrow interpupillary distance has to converge less than the adult with his wide interpupillary distance when fixating an object at a distance of 1 m., yet both infant and adult converge 1 meter angle (Fig. 2).

The defect of the meter angle concept lies in the fact that it obscures the necessity for and the importance of evaluating the actual angle of convergence required for binocular fixation. This is derived by multiplying the interpupillary distance in centimeters by the dioptric distance of the object of regard. Thus an emmetropic subject with an interpupillary distance of 6 cm. must converge 6^{Δ} to fixate an object binocularly at a distance of 1 m. (Fig. 3). If his inter-

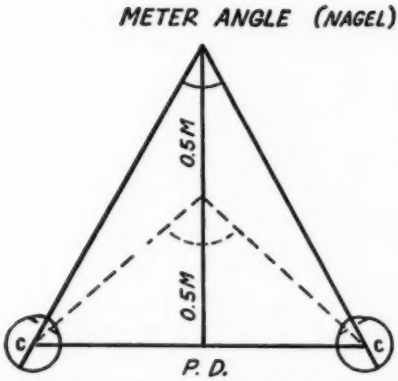


FIGURE 1. Meter angle as conceived by Nagel. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth., 1957, *61:* 375.)

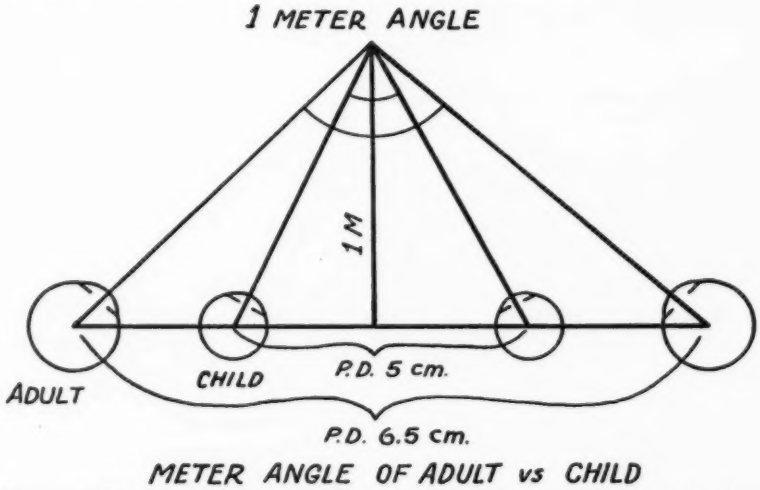


FIGURE 2. Meter angle showing significance of the interpupillary distance in the convergence of an infant and an adult. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth., 1957, *61:* 375.)

pupillary distance is 5 cm. he must converge 5^{Δ}; if 7 cm. he must converge 7^{Δ}. At $\frac{1}{3}$ m. the dioptric distance is 30^{Δ} and the subject with an interpupillary distance of 6 cm. must converge 180^{Δ}, while an interpupillary distance of 7 cm. demands convergence of 21^{Δ} (Fig. 4).

The accommodative *effort* elicited by the stimulus is the key to the amount of convergence elicited, and not the stimulus *per se* and not the amount of accommodation which actually occurs. Accommodative convergence is roughly proportioned to the effort but is generally several diopters short of the convergence requirement for binocular single vision. Thus the subject with an interpupillary

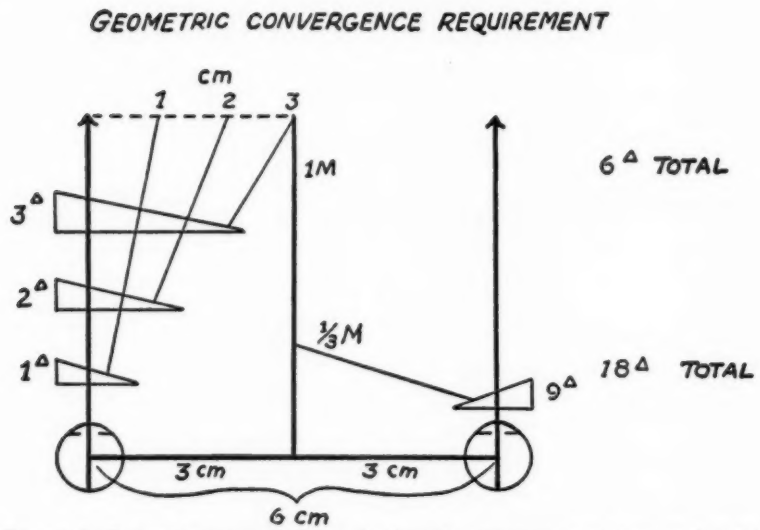


FIGURE 3. Geometric representation of prismatic convergence at 1 m. and at ⅓ m. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth., 1957, *61:* 375.)

distance of 6 cm. if 1 D. hypermetropic must converge 6^{Δ} at 1 m. (6 cm. $\times$ 1^{Δ}) and at ⅓ m. must converge 24^{Δ} (6 cm. $\times$ 4^{Δ}) (Fig. 5). The hypermetropic subject thus will overconverge for a given distance, but through the corrective fusional reflux may retain single binocular vision. He thus exhibits esophoria. If the fusional reflex is inadequate he manifests an esotropia. The excessive convergence response can be removed or reduced by correction of the near refraction with bifocals or the unburdening of cortical accommodation by substitution of peripheral accommodation by the use of diisopropyl fluorophosphate.

In general the convergence elicited by accommodation is not sufficient to permit binocular fixation of the object of regard. It is the function of fusional vergence to take up the slack in the fusion free position and to bring the eyes into exact alignment on the object of regard. The stimulus to fusional vergence is the retinal disparity of the images. Thus a vergence movement stimulated by accommodative effort provides the coarse adjustment, and fusional vergence provides the fine adjustment, of the visual axes for normal binocular single vision at near ranges (Fig. 6).

In accommodative esotropia the eyes are in an overconvergent position in response to the excess of accommodative convergence. The corrective fusional movement is one of divergence, an active and opposite movement to restore binocular single vision. This is an active mechanism and not merely a relaxation of convergence. It is termed relative fusional divergence because a considerable vergence movement can take place without alteration in accommodation (Fig. 7). Relative fusional divergence can be measured directly with prisms and a fine fixation target, or indirectly by determining the weakest plus or strongest minus

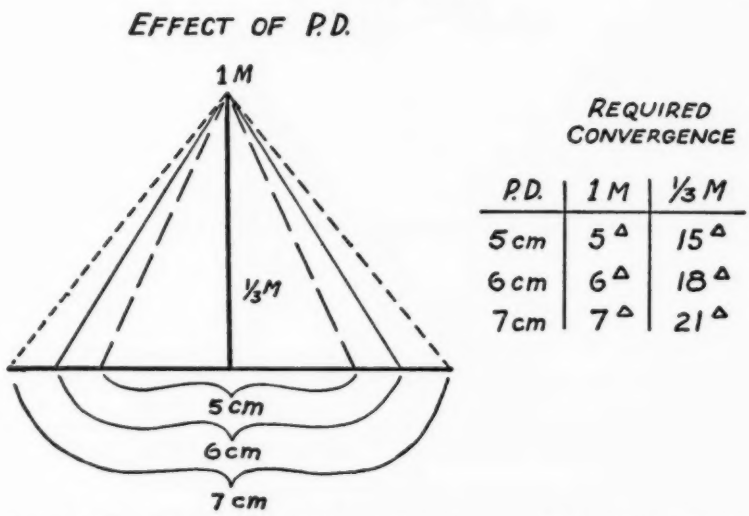


FIGURE 4. Effect of convergence of interpupillary distances of 5, 6 and 7 cm. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth., 1957, *61:* 375.)

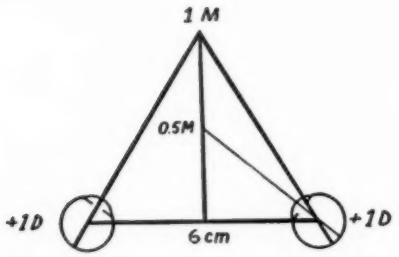
lens permitting binocular single vision at a given focal distance. It is the presence and adequacy of relative fusional divergence which determines whether a given patient can or cannot overcome an excessive amount of accommodative convergence. If fusional divergence is inadequate, the deviation becomes manifest as accommodative esotropia.

A typical history of accommodative esotropia is that of a deviation first becoming manifest when the child is about 2 years of age or slightly older. It may appear as early as his eighteenth month, or as late as his fifth year. Often other members of the family have had this anomaly. At first the parents note the deviation only when the child looks at a near object or when he is tired or acutely ill. Occasionally, the deviation suddenly becomes manifest and persists, but typically it disappears when the child is daydreaming or is not accurately fixating an object.

Then over a period of weeks or months the deviation tends to become persistent for both distance and near fixation. At this stage the magnitude of the deviation is usually variable, but it is seldom as great as in esotropia of the congenital type. The most commonly reported range is from 20 to 30$^{\Delta}$.

Hypermetropia of more than the average amount is the most typical finding associated with accommodative esotropia. As long as it remains uncorrected, the deviation is characteristically greater in near than in distance vision.

In a series of patients with accommodative esotropia, the average amount of hypermetropia present will be greater than that in a comparable group of children with normal binocular single vision. Also, it is a matter of record that anisometropia and astigmatism of high magnitude are more frequent. This is not to imply that every case of accommodative esotropia has a large refractive error.



HYPEROPIC SUBJECT	1 D 1 M	P.D. 6 cm ⅓ M
ACCOMMODATES	2 D	4 D
CONVERGES	12 Δ	24 Δ

FIGURE 5. Accommodation-convergence coordinate of hypermetropic subject at 1 m. and ⅓ m. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth., 1957, *61:* 375.)

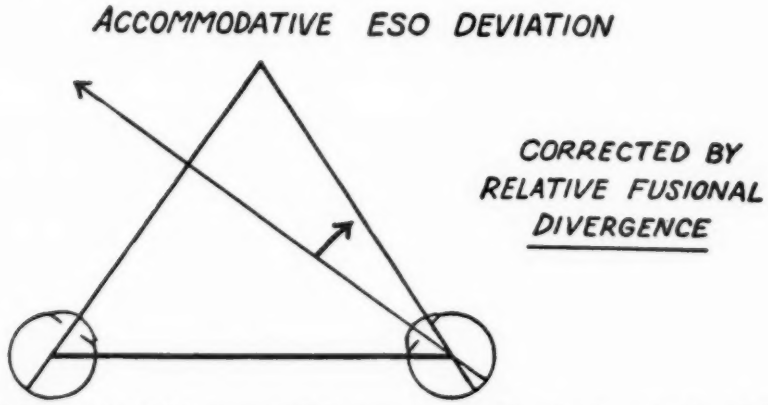


FIGURE 6. A deficit in accommodative convergence giving rise to exotropia: relative fusional convergence. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth., 1957, *61:* 375.)

In fact, children with hypermetropia of 7 D. or more may not develop accommodative esotropia simply because they may make no effort to overcome the hypermetropia by accommodation.

The most important subtype is found in that large group of patients who have a residual esotropia in near vision when the refractive error is corrected. The origin of this excessive accommodative convergence in near vision is not fully established, but multiple factors are probable. For purposes of treatment, these patients are considered to retain an abnormal accommodation-convergence relationship when the patient is made emmetropic with glasses.

Uncorrected hypermetropia may add an accommodative component to an esotropia of any origin. Also it may precipitate esotropia if a sensory obstacle to

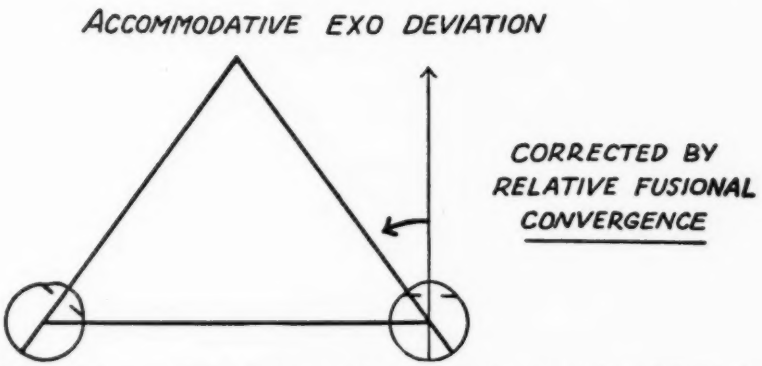


FIGURE 7. Accommodative convergence in excess causing esotropia: relative fusional divergence. (Courtesy of Breinin, G. M.: Tr. Am. Acad. Ophth. 1957, *61:* 375.)

vision such as cataract or congenital amblyopia is present in one eye, or if the patient has a basic esophoria of any origin.

Untreated, the usual course of a typical accommodative esotropia is the development of persistent esotropia of moderate degree. Furthermore, the longer the esotropia persists, the less likely is the deviation to be eliminated by the prescription of spectacles. Also, adaptive sensory and motor abnormalities may develop. A decrease in the amount of esotropia usually occurs as the child grows into adulthood; therefore, spontaneous cures occasionally occur, but they are uncommon. Two groups of patients, those with large refractive errors and those with poor vision, are prone to change from an accommodative type of esotropia in early childhood to exotropia in adolescence.

If a marked anisometropia or irreversible impairment of vision is not present, the prognosis for the cure of accommodative esotropia is good, provided adequate treatment is instituted early and is continued over a period of years. Early treatment is urgent to prevent secondary sensory and motor changes if the child is to maintain his opportunity to develop a normal type of vision. Persistent treatment is necessary in order to maintain good alignment and stable fusional mechanisms during the child's developmental years.

In all cases it is essential to establish and maintain maximal visual acuity by correction of the refractive error. Amblyopia, if present, should be treated by active visual stimulation as well as by occlusion of the preferred eye. Correction of the deviation can be conducted concurrently.

In typical accommodative esotropia a normal accommodation-convergence relationship is restored by the prompt prescription of glasses, fully correcting or even overcorrecting the hypermetropia. If the prescription of glasses has been delayed, an amount of esotropia sufficient to prevent fusion may persist in distant vision. If this basic deviation is constant and other methods have been inadequate, surgical correction of only this amount of esotropia should be considered.

In some atypical cases of accommodative esotropia, an abnormal relationship persists even when a patient is made emmetropic by glasses. The excessive ac-

commodative convergence in near vision can be treated by the prescription of bifocals or miotics, or both. As in typical cases, surgery is indicated only for a persistent and significant basic deviation. In all cases of esotropia having an accommodative component, surgery should be undertaken with great caution, since postoperative exotropia is prone to develop. Surgery should not be undertaken merely to obviate the need for glasses.

In more mature children a variety of orthoptic procedures can be used to develop and stabilize the fusional processes. If relative fusional divergence becomes adequate the strength of the glasses can often be reduced to the minimal amount to maintain comfortable binocular single vision. With early and persistent treatment, it is reasonable to expect that patients with less than 4 D. of hypermetropia can develop some independence from glasses.

Comment: The symposia of the American Academy of Ophthalmology and Otolaryngology are one of its most interesting features, and this is no exception. Breinin's emphasis upon the measurement of the actual angle of convergence is most important. This concept should be stressed as it explains one factor in the so-called hyperconvergent status of childhood; that is, for a fixation distance of 25 cm., a child with an interpupillary distance of 5 cm. requires 20^{Δ} of convergence, whereas for the same fixation distance an adult with an interpupillary distance of 7 cm. requires 28^{Δ} of convergence. It is worth repeating that it is the accommodative effort and not the stimulus to accommodate or the actual amount of accommodation that is the factor associated with convergence. Thus in either the hyperkinetic type of child or the child with a sluggish accommodation mechanism, there will be an excess of accommodative effort with resultant overconvergence.

The clinical classification of the four subgroups is extremely useful. The first subgroup, the "pure" or typical accommodative esotropia, is that in which correction of the hypermetropia eliminates the deviation for distance and near. The panel members properly stress that this is not sufficient. Any sensory adaptations, such as amblyopia and suppression should be actively eliminated. Then secure binocular vision should be established in the hopes of gradually eliminating glasses up to a strength of 4 D.

The second subgroup is that in which single vision glasses eliminate the deviation for distance but a residual esotropia remains for near. When bifocals or miotics fail to eliminate this residual for near, Costenboder advocates cautious single or bilateral recessions of the medial recti, depending on the amount of the basic esophoria. Swan advocates judicious delay, feeling that many of these cases will correct themselves as their interpupillary distance widens, their arms lengthen and their usual hypermetropic refractive error becomes less. Certainly this is a difficult question to answer. Surgery can give gratifying early results, but I know of no sufficiently long follow-ups to give a positive answer. Neither have I had the opportunity to see if these cases will outgrow the defect. My own treatment of these cases has been dependent upon the amount of suasion extended by the parents to have the cosmetic defect corrected. When they have been insistent, a cautious recession of each medial rectus has been the operation selected. Some are apparently "cured" whereas in others there is overcorrection of the divergence excess variety shortly thereafter. These have been corrected with recessions of the lateral rectus muscles.

The panel advocates extreme caution in handling cases with an extreme amount of hypermetropia or an insuperable amblyopia due to anisometropia or organic defect. This applies to all cases of esotropia whether they are accommodative or not, since such cases are prone to develop divergence as reported by Dunnington and Regan a few years ago.

PHILIP KNAPP

INFLUENCE OF THE FIFTH CRANIAL NERVE ON THE INTRAOCULAR PRESSURE OF THE RABBIT EYE

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Brit. J. Ophth., 1957, *41:* 257–300

The mechanism by which the normal intraocular pressure is maintained has excited the interest of physiologists and ophthalmologists even since the association between an increase in this pressure and the disease known as glaucoma was first pointed out. In considering the many factors concerned in the maintenance of a constant intraocular pressure, it must be remembered that, although a mechanical analogy may be used to explain the broad principles of control of the intraocular pressure, it proves deficient when applied to the details of the actual apparatus found in the eye. First, the blood vessels are far from being a rigid system of tubes, and it is probably true that the capillary bed of the ciliary body, which brings the blood into contact with the blood-aqueous barrier, is never fully open or closed but that different parts of it are dilated or contracted in a constantly varying proportion. Second, it has been shown that aqueous humor is produced by a process involving secretion—an activity which is always under some form of central control, either hormonal or nervous; and third, it must be remembered that the aqueous humor is not solely concerned with the maintenance of intraocular pressure, but has metabolic duties to perform in relation to such avascular structures as the lens and the cornea. It seems reasonable, therefore, to assume that some form of control over the formation and flow of the aqueous and over the intraocular pressure must exist.

Once the need for a controlling mechanism is admitted, it is natural to think of the central nervous system as a possible participant, in spite of the fact that considerable autonomy exists in the peripheral vascular system. Evidence has been found to show that the autonomic nervous system may play a part in the control of intraocular pressure through sympathetic pathways. Probably the most important effect of the sympathetic, as demonstrated by earlier experiments, is the vasoconstriction it produces in the ocular blood vessels.

Another type of vascular response associated with nervous activity is that found in relation to the sensory nerves, and the present study was undertaken to determine whether vascular changes leading to changes in intraocular pressure could be mediated by the sensory supply to the eye. This possibility was investigated by cutting and stimulating the fifth cranial nerve in rabbits. The results of these experiments may be summarized as follows:

(1) Mechanical stimulation of the intact fifth nerve caused, on the side of stimulation, a contraction of the pupil, a rise in the temperature of the ciliary

region, a rise in intraocular pressure, and an increase of protein in the aqueous humor.

(2) In the contralateral eye, no contraction of the pupil resulted from stimulation of the opposite intact fifth nerve, but a rise in intraocular pressure occurred in 15 per cent of the animals. In half the experiments an increase in protein was found in the aqueous humor of the contralateral eye, and in six out of eight animals a rise in the temperature of the ciliary region was recorded.

(2) Section of the fifth nerve produced the same immediate effects as stimulation. Although the tension of the eye on the side of section tended to be slightly lower than that on the normal side when measured from two to four weeks later, the differences were not statistically significant.

(4) Stimulation of the fifth nerve caused a vasodilatation of the episcleral vessels of the ipsilateral eye. No change was found in the choroidal vessels of this eye.

(5) In animals in which the fifth nerve had been sectioned from two to four weeks previously, stimulation of the cranial portion of the nerve caused no changes in the pupil or the intraocular pressure.

(6) Histologic examination of the nerves previously sectioned showed degenerated fibers in that part of the nerve central to the section. These fibers probably arose from ganglion cells in the trunk of the fifth nerve peripheral to the point of section.

(7) It appears, therefore, that the vascular changes in the eye which follow antidromic stimulation of its sensory nerve supply are comparable to the vascular changes in the skin which follow antidromic stimulation of the peripheral sensory nerves.

Although these experiments show that the fifth cranial nerve in rabbits can mediate impulses for raising the intraocular pressure, this does not necessarily imply that the nerve takes an active part in the normal control of intraocular pressure. The fact that animals in which the nerve had been divided some weeks previously showed little change in ocular tension is against such a suggestion, but does not exclude it. It may well be that the intraocular pressure is to some extent self-regulatory under normal conditions, and that the nervous mechanisms are only brought into action when the equilibrium is disturbed. Under pathologic conditions, however, it is probable that local irritative lesions in the eye stimulate the fifth nerve endings, cause reflex vasodilatation, and raise the intraocular pressure. Lesions that stimulate the trunk of the ophthalmic division or the Gasserian ganglion might also cause similar changes. It must be emphasized, however, that the results of experiments performed on rabbits cannot be applied unreservedly to the human eye.

Comment: This article is a continuation and elaboration of the work published by Perkins in 1935 in which he showed that mechanical stimulation of the fifth nerve caused vasodilatation, a marked rise in ciliary body temperature and a large rise in intraocular pressure. The effects could occur in the contralateral eye. In addition, in this paper Perkins presents an excellent review of the evidence to date of the relation between the various components of the peripheral nerves and the ocular circulation, and the relation between trauma and intraocular pressure.

The evidence that the fifth nerve in the rabbit probably does not contain sympathetic fibers before the nerve enters the orbit makes Perkins' experiments particularly valuable since sympathectomy permits rather definite conclusions.

The contralateral effects are most interesting and suggest, from the ciliary body temperature rise, the vasodilation occurs in a high proportion of instances. Since it occurs in sympathectomized animals, it certainly does not follow the sympathetic pathway. A direct central pathway seems to be the most likely one.

Two important questions may be asked after this stimulating work: (1) What is the nature of the central nervous reflex, direct or through vasocontrol? (2) If direct, what is the nature of the peripheral control? The work being described in relation to trabecular nerve supply and the nature of the trabecular resistance to aqueous outflow may help answer these questions.

H. Saul Sugar

PROBLEMS ASSOCIATED WITH DIAGNOSIS AND THERAPY OF GLAUCOMA

W. Leydhecker

Docum. ophth., 1956, *10:* 174–243

A survey of the provocative methods has proved Priscoline to be the most reliable, whereas the results of the caffeine and water drinking tests depended markedly on the initial tension. The advantages of electrotonography were emphasized on the basis of the results of the author's personal studies concerning early diagnosis of glaucoma. He called attention to the possibility of adulteration of the results by the after dilatation of the coverings of the eyeball, depending on the degree and duration of the demands made on it as described by Goldmann. He suggested that tonography be performed for 5 minutes, the first minute being excluded in the evaluation of the results. For better separation of the normal from the glaucomatous eyes the term "outflow value" was introduced, which as a quotient expresses the relationship between the value P_o (intraocular pressure before the onset of tonography) and the value C (reciprocal value of outflow resistance). Furthermore, the suggestion was made to use the term "differential tonography" for the type of tonography performed with various weights.

Studies revealed that on rising in the morning the tension immediately decreased by 4 to 6 mm. It seems, therefore, advisable to take the morning-measurements in bed, before rising.

The need for careful control of both eyes, even for prolonged periods after an injury, was emphasized, since glaucoma is also observed in the undamaged eye of patients with secondary glaucoma following contusion or perforating lesions. Because of the high incidence of glaucoma of both eyes in patients with unilateral central vein thrombosis, a vascular sclerosis has been considered as a common cause of thrombosis and glaucoma, particularly since comparative observations

by the internist also seemed to favor it. Routine tonometry performed at the polyclinic in 1950, first on completely unsuspected eyes, revealed definite glaucoma in 7 per cent of the patients, among whom there were patients between the ages of 10 and 19 years (3.2 per cent). It is recommended that tonometry should be performed in every patient.

In the simultaneous occurrence of glaucoma and cataract, cataract operation was performed up to a pressure of 45 mm. Hg. Cyclodyalysis was given preference over fistula forming operations in patients with higher pressure values if an angle of the anterior chamber was open.

DISCUSSION

Goldmann (Bern, Switzerland) stated that little is known at present about the mechanism of glaucoma. He raised the question whether damage to the fibers of the optic nerve alone is to be considered as a sequel of the increased pressure, or whether it may occur independently of it, or whether the increased pressure in combination with other factors may cause decrease of the visual field. He reported on personal studies concerning the problem of relationship between increase in ocular pressure and later damage to the visual field; results showed that secondary damage to the optic nerve may result from an increase in ocular pressure by way of a circulatory disturbance. Under certain conditions, disturbances of blood perfusion may occasionally cause a similar decrease of the visual field without any increase in pressure. Goldmann emphasized the necessity of exact tonometry with simple, precise tonometers, this making it possible for even the practitioner to make an early diagnosis of glaucoma, since tonography cannot be performed routinely outside the clinic.

Schmidt (Bern, Switzerland) reported on experiences with testing of Schiötz' tonometers in the new testing department of the ophthalmologic clinic of the University of Bern.

Franceschetti (Geneva, Switzerland) considers the introduction of the value *R* (value of outflow resistance) for the clinical evaluation of tonography of greater practical usefulness than the previously used term *C*, which gives the reciprocal value of the outflow resistance and which must be expressed in number values that constantly become smaller when the outflow resistances become higher. Attention was called to cases of glaucoma in patients with high myopia who present an apparently completely normal ocular pressure. Franceschetti also emphasized the strong influence exerted by the environmental demands on the pressure conditions of a glaucoma which has been well controlled in the hospital.

Sourdille (Nantes, France) reported satisfactory results with primary operative reduction of tension and successive extraction of cataract. He believes that operative reduction of tension, particularly by way of iridencleisis, is indicated even in glaucoma with progressive narrowing of visual field.

Nordmann (Strassburg, France) reported a case to illustrate the strongly provocative effect of the environmental influences on the intraocular pressure conditions, which may cause considerable difference between ambulatory measurements and those made in the hospital. Careful study of the base of the skull, the

carotid arteries, and the retinal circulation is to be considered as indispensable in patients with so-called glaucoma without increased pressure. He explains a decrease of the visual field which progresses after operative reduction of pressure as being caused by an irreversible disturbance of the regulatory mechanism. Results of therapeutic trials with Maxiton were reported. Improvement in the visual field could still be obtained in cases of glaucoma with extensive reduction of the visual field.

Francois (Ghent, Belgium) established a direct relationship between depth of anterior chamber and outflow resistance in an experimental study on eyes in cadavers.

Harms (Tübingen, Germany) emphasized the individual peculiarities of each case of glaucoma which prohibit schematic proceedings. He recommended the so-called instillation curve.

Hager (Tübingen, Germany) reported results of routine night measurements, which make possible the detection of glaucomas with pressure peaks during the night, so-called "night types."

Sautter (Hamburg, Germany) pointed out that in evaluating the results of tolerance tests the various types of production of glaucoma must be taken into consideration in the individual patient. He confirmed the speaker's statements concerning glaucoma and thrombosis of central veins.

Rosengren (Gothenburg, Sweden) reported on the effect of neostigmine in glaucoma refractory to pilocarpine. Neostigmine exerted a better pressure reducing effect in many cases but this effect was only temporary. The question was raised whether there have been satisfactory experiences with Mintacol.

Comment: Leydhecker's introduction of the outflow ratio P_o/C in tonographic evaluation of the glaucoma has aroused considerable interest among workers in the United States. (The symbol P_o is the intraocular pressure before the beginning of tonography and C is the coefficient of aqueous outflow or the reciprocal outflow resistance). If the numerical value of P_o/C is over 100, it is probably glaucoma. It must be pointed out that no matter what formulas and ratio we use, our search for the absolute yes or no—that is, is it glaucoma or is it not?—will be answered by some uncertainty in equivocal borderline cases which will have to depend on observation over a period of time.

The fact that on rising in the morning the tension rises somewhat is understandable physiologically. It emphasized a related point, that there is a difference of 1½ to 2 mm. in tension when the patient is lying down as compared to that in the sitting position, when an applantation tonometer is used. The tension in the lying position is higher, probably a manifestation of the venous pressure variation.

Leydhecker's statement, that because of the high incidence of glaucoma in both eyes of patients with unilateral venous thrombosis vascular sclerosis has been considered as a cause for both glaucoma and thrombosis, evokes interest in this editor because this idea was first published by him (Sugar, H. S.: Arch. Ophth., 1942, *28:* 587). It was then corroborated by Wessely (von Graefes Arch. Ophthal., 1947, *148:* 111, and was further considered by this editor (ACTA Conc. Ophth. XVI, Britannia, 1950, 846). The purpose of these articles was to relate the sclerotic factor with glaucoma simplex.

The question of cataract and glaucoma depends a little on the type of glaucoma. In simple glaucoma it is true that the lens can be removed first, especially with the preopera-

tive use of Diamox. In this type of glaucoma a difference of opinion is natural since both methods give good results. In acute congestive attacks of angle closure glaucoma, the tension should receive first consideration. In interim situations, it should be remembered that removal of the lens deepens the anterior chamber and, if the angle is open, one may consider the angle closure mechanism as cured.

The work of Goldmann on the relation between the field and optic nerve changes in glaucoma should be brought to the reader's attention (Gafner, F., and Goldmann, H.: Ophthalmologica, 1955, *130:* 357). He points out that the disk is provided with a separate blood supply, the central artery of the optic nerve, and is not connected with the central retinal artery. Pressure changes or sclerotic change may involve the tiny vessels on the disk and in the nerve and cause loss of blood supply to the nerve fibers and atrophy of the glial structure with subsequent field changes and disk excavation. Thus one can see why in young glaucoma patients, especially the juvenile ones, disk changes always follow increase in pressure whereas in some old glaucoma patients, field changes are often concomitant and even out of proportion to the duration and degree of increased intraocular pressure. Also, from this one can explain the decrease in field in hypertensive patients once they are given drugs to reduce markedly the arterial pressure.

H. Saul Sugar

DIFFERENTIAL DIAGNOSIS OF SECONDARY GLAUCOMA

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Glaucoma may be considered secondary when it can be attributed to a pre-existing ocular condition or disease which has caused a temporary or definitive interference in the circulation of the aqueous. Glaucomatous conditions may, however, occupy various positions between the true primary and secondary glaucomas, and it is in connection with these intermediate forms that the greatest scientific difficulties arise and that the differential diagnosis becomes most perplexing.

Perhaps the best illustration of these difficulties is that afforded by the Posner-Schlossman syndrome of glaucomatocyclitic crises, a clinical entity characterized by recurrent monocular hypertensive attacks, associated with signs of a mild cyclitis, in eyes with open angles. The prognosis is benign and the attacks, which occur at intervals, are separated by remissions during which the condition of the eyes apparently returns to normal, biomicroscopically, gonioscopically, and tonographically. It seems as though the glaucoma is not a result or a complication of the uveitis, but rather that both are concomitant expressions of a single disease entity, the nature of which is not yet known. Although this syndrome possesses characteristics suggestive of narrow angle glaucoma (acute) or of

glaucoma secondary to uveitis, it presents certain identifying features by which it may be distinguished from these conditions. It is unilateral and the recurrences always occur in the same eye; generally there is no pain, only discomfort and colored halos; vision is normal or only slightly decreased if corneal edema is present; the eye is white; the pupil slightly dilated, regular, and with good reflexes, whereas in glaucoma secondary to uveitis it is small and irregular; posterior synechias do not occur; the angle is of normal width and remains open during the attack and no material is deposited over it, as is the case in glaucoma secondary to uveitis. Tonography during the attacks shows impairment of the drainage of the aqueous without any great alteration in its production. During the periods of remission the drainage not only becomes normalized but may even be greater than in the other eye, with relative hypotony. The optic nerve remains normal even in cases in which the attacks have been numerous. In glaucoma secondary to uveitis, moreover, the keratitic precipitates are more numerous, they may or may not be pigmented, and generally they are seen only when the uveitis is active, whereas in the Posner-Schlossman syndrome they are nonpigmented and relatively scarce.

Aphakic glaucoma may be an obvious consequence of operative or postoperative complications such as delayed formation of the anterior chamber, loss of vitreous, or uveitis, or it may occur without any apparent cause. Clinically, it is characterized by a progressive increase in tension, excavation of the disk, typical glaucomatous changes in the visual fields, a deep anterior chamber, an open angle, generally without special characteristics, and difficulty in the drainage of the aqueous during tonography. Examination of the other eye in cases of aphakic glaucoma often reveals drainage difficulties, in addition to other signs of wide angle glaucoma (chronic), which probably existed also in the eye that underwent operation. In such cases, operation acts as a provocative test by further reducing drainage capacity and so producing a composite picture in which a secondary glaucoma is superimposed upon one that is primary. Too much stress cannot be laid on the importance of using every possible preoperative test before operating on the eye in order to prevent avoidable surgical damage. Tonography, in particular, should always be used as a routine measure.

Glaucoma resulting from late formation of the anterior chamber in eyes that were normal before surgical extraction of cataract usually begins in a gradual or subacute manner some 6 or 10 weeks after the operation in cases in which the reformation of the anterior chamber has been delayed for not less than 7 days. Clinically, it may be slight, moderate or severe and the appearance of the goniosynechias may vary from the conical or trapezoid type that includes the corneoscleral trabeculum and even, sometimes, the cornea, to those that join and may practically close the entire angle, annulling the drainage facility. Among the most interesting of these cases are the slight ones in which the tension may rise to about 45 mm. Hg, generally with pronounced daily fluctuations of an inverted type. The values of the coefficient of the drainage facility are between 0.05 and 0.10, and they maintain this level constantly, regardless of the daily fluctuations of tension, sometimes even for years. Cases of this type respond very

favorably to the anticholinesterase miotics and especially to diisopropyl fluorophosphate (DFP), the reduction of tension paralleling the increase in facility of drainage and the cessation of the daily fluctuations. Treatment with DFP given every 3 days can control a case indefinitely and in some patients it will even bring about a clinical cure. Prolonged postoperative observation of the anterior chamber is therefore important, and Kronfeld goes so far as to say that every anterior chamber that is slightly shallow or even only moderately deep after a cataract operation should be regarded as abnormal.

The association of thrombosis of the central retinal vein with preexisting glaucoma seems to be more than a mere coincidence. Two types of glaucoma are found in eyes with venous occlusion: one is acute and hemorrhagic and occurs after a latent period, with high tension, rubeosis of the iris, and a poor prognosis, generally ending with enucleation; the other, more benign, is nonhemorrhagic, with no previous latent period, and is unaccompanied by rubeosis. Histopathologic studies seem to show that the thrombosis is not an isolated phenomenon, but rather one that forms part of a diffuse ocular picture in which the endothelium is chiefly affected and which bears a close resemblance to that observed in diabetes, angiosclerosis and prolonged hypertension. The relationship, therefore, between venous occlusion and glaucoma is not necessarily one of cause and effect. Both conditions may occur independently in eyes affected by vascular changes; or the second, nonhemorrhagic, type of glaucoma may be not the effect but the cause of the occlusion.

The clinical course of glaucoma associated with pseudoexfoliation of the crystalline lens is very similar to that of chronic open angle glaucoma. It may, however, be effectively differentiated by biomicroscopy and gonioscopy, which shows an open angle, slightly veiled by material deposited on it, and a trabecular ring of pigment caused by the deposition of pigment granules. Glaucoma associated with hypermature cataract is correctly termed phakolytic. It does not seem to be caused only by rupture of the capsule; degeneration also seems to be a sufficient cause, inasmuch, as it makes the lens permeable to the products of cortical hydrolysis. This type of glaucoma is preventable, but if it occurs it can be treated successfully by extraction of the lens and rinsing of the anterior chamber. Total recovery is often obtained by this means even in cases in which light perception was lost.

Chronic glaucoma with a closed angle (chronic congestive glaucoma) may well be included among the secondary glaucomas, since it is really a sequel to narrow angle glaucoma that has not been adequately controlled during attacks and that has, therefore, led to the formation of synechias and trabecular changes apparent on gonioscopy. This type of glaucoma may be expected to disappear in time as a result of the use of modern drugs during the hypertensive attacks. Its appearance in the future may even be considered as a sign of negligence in treatment.

Comment: The idea that glaucomatocyclitic crisis is "not a result or a complication of the uveitis, but rather that both are concomitant expressions of a single nosological entity . . ." is continuing the idea of an intermediate position of the disease in our classification. Since it is part of the group of glaucomas associated with uveitis, by definition it is secondary, especially until we learn more about them.

It is recommended that those interested in the relation between simple glaucoma and venous occlusion should refer to the papers of Moore, Wessely and Sugar.

The material on pseudoexfoliation brings out again the problem of our failure to clinically corroborate such a condition. The same idea was presented by Busacca in 1927 to 1930. He held that the material on the lens capsule was a granular, membrane-like precipitation of substances normally found in the aqueous. His views, which were based on sections of three eyes, were refuted in 1931 by Grzedzielski, who showed, by sections of normal eyes, that the precipitates found on the capsule are artefacts that may be present in any fixed normal section. I believe that long fixation may be a factor in its production and that there is no such entity clinically.

In discussing chronic angle closure glaucoma, Trujillo proposes the inclusion of chronic angle closure glaucoma amongst the secondary glaucomas because it is really a "sequella originating from narrow angle glaucoma." I would object to such a proposal since we must avoid confusing variations resulting from physiologic differences with actual etiologic differences.

H. Saul Sugar

The Retina and Vitreous

THE VITREOUS: GROSS AND MACROSCOPIC OBSERVATIONS SEEN IN AGE AND DISEASE WITH SPECIAL EMPHASIS ON THE ROLE OF VITREOUS IN DETACHMENT OF THE RETINA

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The normal vitreous is a transparent gel that completely fills the posterior part of the eye. It acts as a cushion to keep the structures of the eye in their normal position. Its cushioning effect helps to keep the retina in contact with the pigment epithelium. In the young adult without a history of disease, the vitreous has its normal characteristics. With age, however, certain changes take place in the vitreous in the form of shrinkage, liquefaction, and formation of strands. Such changes in themselves may have no adverse effect on the general health of the eye. On the other hand, certain relatively minor changes associated with the usual senescent processes may result in serious complications.

During the process of opening the globes sent to the pathology laboratory at the Institute of Ophthalmology, Presbyterian Hospital, it was observed that certain changes found in the vitreous fell into a general pattern depending on age, history of ocular disease or injury. These changes have been described by many authors, but their relative importance has been minimized because they have usually been regarded as artefacts. On further investigation, however, it

became clear that most of the changes were not artefacts but had existed before the eyes were enucleated. Both fresh and fixed normal globes from young persons, when opened, showed the vitreous to be transparent, normal in its consistency, and at all times filling the vitreous cavity. Other globes, from persons with a history of ocular disease, when opened showed typical changes in the vitreous corresponding with the type of the disease. Where there had been a perforating wound that extended into the vitreous cavity, it was generally possible to follow the course of the perforation by a condensation and a loss of transparency of the vitreous. The course of an intraocular foreign body could often be traced by the thin line of opaque vitreous extending from the point of entry and coursing to the site of the foreign body. In cases of this kind, in which the vitreous has been damaged by a perforating wound or an intraocular foreign body, the vitreous becomes liquefied and often leaves localized areas of condensation in the form of dense vitreous strands. If there has been an associated inflammation, the strands become cellular and later contract. The contraction of the strands often results in a detachment of the retina.

In order to interpret many of the routine changes found in the vitreous, it is necessary to study the eye in youth and in age, because typical changes take place in the vitreous of elderly patients. With age, the vitreous tends to shrink and to become detached posteriorly. The superior portion of the vitreous is usually the first to become detached. The posterior hyaloid can often be seen with a slit lamp. As the vitreous continues to shrink, the space left between the retina and the hyaloid becomes filled with a fluid substance resembling the aqueous. Further detachment of the vitreous extends to the region of the equator, but the attachment of the hyaloid to the optic nerve remains. Later, however, the attachment of the vitreous to the optic nerve separates and the posterior detachment of the vitreous is then complete. Oftentimes such a detachment can be seen clinically, identified by a circular opacity undulating on the posterior surface of the hyaloid. In the absence of previous ocular disease such shrinkage of the vitreous may have no damaging effect on the eye. When the vitreous first becomes detached, however, there are symptomatic manifestations in the form of lightning flashes. These symptoms have been explained by the fact that the floating vitreous strikes against the retina after rapid movement of the eye, causing stimuli that are interpreted as lightning flashes. Further shrinkage of the vitreous will result in the disappearance of these troublesome symptoms.

Detachment of the vitreous is a common finding in eyes from patients older than 50 years of age. In patients above the age of 65, shrinkage of the vitreous was found in between 70 and 75 per cent of the eyes examined. Simple shrinkage of the vitreous cannot be associated with other pathologic changes in the eye, but there are conditions in the eye which may hasten or cause changes identical with those seen in elderly patients. In cases of myopia, shrinkage and liquefaction of the vitreous may develop, and numerous floating strands can often be seen both clinically and macroscopically. These changes in themselves may cause no damage to the eye, but if there is an adhesion of the vitreous to the retina, subsequent shrinkage of the vitreous may result in a retinal tear as a consequence of localized traction. Condensation of the vitreous may be followed by contrac-

tion of the strands leading to a retinal tear and subsequent detachment of the retina.

These facts show that the vitreous plays a dominant role in the process of retinal detachment. Among the conditions that render retinal tearing likely are the presence of small atrophic areas in the retina and the existence of small points of chorioretinitis. Holes of different types may be found in the retina after detachment. The usual horseshoe shaped tear is probably caused by traction of a retinovitreous adhesion on a weakened section of the retina. Small secondary holes are probably caused by the outward pressure of the subretinal fluid on small areas of chorioretinitis as it migrates to the lower portion of the globe. In recent years, improved methods of examining the peripheral fundus have revealed many small holes unaccompanied by detachment of the retina. These holes may be the result of small cysts in the periphery, and they may remain unchanged without even causing a detachment so long as the vitreous cushions this area. Cystic changes of this kind have often been blamed for detachments of the retina, but a better understanding of the changes found in the vitreous, clinically, macroscopically, and microscopically, leads to the conclusion that they cannot be considered a major cause of retinal detachment.

In cases in which hemorrhage occurs and extends into the normal vitreous, the blood remains dark and in dense strands, causing a prolonged diminution of vision. Absorption in such cases may take months or even years. It is not unusual, however, to see a patient with a recent vitreous hemorrhage that clears within 24 to 48 hours. A hemorrhage of this kind probably takes place in the retinovitreous space. The eye in a case of this kind probably has a detachment of the vitreous with shrinkage, and the blood escapes into the area containing fluid behind the vitreous. Blood in this fluid medium settles rapidly and the return of vision may be prompt.

The characteristics of subretinal fluid vary with the nature of the disease process in the eye. If there is a serous detachment of the retina with a hole, the subretinal fluid remains liquid and does not coagulate on fixation. On the other hand, in the presence of a choroidal tumor with a secondary detachment of the retina and no hole, the subretinal fluid is high in protein and coagulates quickly on fixation. The same coagulability of the subretinal fluid is seen in inflammatory conditions causing detachment, for example, Harada's disease, toxemia of pregnancy, and localized chorioretinitis. This clearcut difference in the characteristics of the subretinal fluid might easily help to establish the diagnosis in certain cases.

Comment: During any kind of intraocular operation it is well to know the condition of the vitreous, which should be studied beforehand, if possible. Usually one thinks of the importance of a pathologic alteration of the vitreous, but sometimes one has to modify an operative technic because the vitreous is normal. A traumatic retinal disinsertion, for instance, poses a different surgical problem in an eye with normal vitreous than in one with liquefied gel. When normal vitreous has herniated into the subretinal space, the barrage of diathermy punctures has to be placed further back, well behind the herniated vitreous, in order to secure an effective chorioretinal adhesion.

BERTHA A. KLIEN

OCULAR MANIFESTATIONS OF SOME VASCULAR DISORDERS IN THE AGED

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Among the many afflictions associated with advancing age, the most tragic may be loss of vision. Cataract and glaucoma are well known afflictions, but less familiar are disorders of arteries.

OCCLUSION OF CENTRAL ARTERY OF RETINA

Immediate blindness of the affected eye results when the central artery of the retina is occluded. The ophthalmoscopic picture is distinctive: narrowing of the arterioles, segmentation of the column of blood in the arterioles and veins, whiteness of the retina, and a red spot at the fovea. The whiteness of the retina, a result of ischemic edema, fades away in about 10 days to 2 weeks. The retinal arterioles may become widened within a few hours to a few days; and then after several weeks, as optic atrophy ensues, they become attenuated.

The central retinal artery may be occluded by thrombus, embolus, or spasm. Thrombosis superimposed on an atheromatous plaque characteristic of sclerosis, either senile or hypertensive, appears to account for the largest number of closures. A common site of interruption is at the passage of the artery through the lamina cribrosa sclerae. A sclerotic plaque partially blocks the flow of blood, slowing it, and formation of a thrombus completes the occlusion. Embolism accounts for some occlusions of the central retinal artery. Too frequently the source of an embolus remains obscure. Spastic constrictions may be superimposed on sclerotic plaques, on thrombi, or on emboli as a result of local irritation. They occur also in hypertensive disease, partly through localized areas of arteriosclerosis and partly through narrowing of the lumen of the artery in association with the heightened blood pressure.

Treatment at present is limited to the employment of vasodilators, anticoagulants, oxygen and carbon dioxide. Since in many cases improvement occurs spontaneously, evaluation of any therapeutic agent is difficult, and some observers doubt the value of any of these measures. Obviously there is no effective way of removing an atherosclerotic plaque from the central retinal artery. As an attempt to relax the spasm in an artery, a solution of papaverine hydrochloride, ½ to 1 grain (0.032 to 0.065 gm.), may be administered intravenously. At least it is an effective dilator of peripheral arteries. For the purpose of preventing formation of a thrombus, heparin injected intravenously is the best agent available for immediate effect. Administration of bishydroxycoumarin (Dicumarol) by mouth may be started at the same time; and after two days, when enough is absorbed to be effective, it can replace the heparin. The length of time that anticoagulants should be given is controversial.

Oxygen in high concentration might be of benefit to a retina previously de-

prived of it, and carbon dioxide is a vasodilator. A mixture of 95 per cent oxygen and 5 per cent carbon dioxide administered through a mask for the first hour might be given a trial. If it appears to restore or improve vision, it may be continued for as long as 24 hours. As its continuous administration for many minutes causes restlessness and confusion, its administration must be interrupted occasionally—perhaps several times an hour—with periods of rest, the patient inhaling the mixture as much of the time as he can with comfort.

Spontaneous Thrombosis of Internal Carotid Artery. Spontaneous thrombosis of the internal carotid artery and its resulting ocular manifestations arises from thrombus of an atherosclerotic plaque in the carotid sinus at the origin of the internal carotid artery. Upon the plaque a thrombus forms which gradually narrows the lumen of the artery. As the artery becomes more and more occluded, the pressure of the blood in the branches is reduced and its flow is slowed, with consequent symptoms of vascular insufficiency.

Although there is no regular, consistent sequence of events in this disease, a certain pattern of symptoms should arouse the suspicion of the examining physician. Some of the patients have repeated transient episodes of blindness in one eye, followed after a few weeks or months by paralysis of the opposite side of the body. The episodes of monocular blindness last from a few seconds to a few minutes and may recur several times a day or at intervals of as long as several weeks. In a few instances vision has not returned and the eye has remained blind. The pathologic basis of these episodes, as distinct from the disease as a whole, is not known. After a time—perhaps a few months—a clot forms in one of the cerebral branches of the internal carotid artery, causing paralysis of the opposite half of the body and in some instances homonymous hemianopsia. After the stroke the transitory episodes of blindness ceases.

The ocular fundi most often appear normal; occasionally on the affected side there may be large soft exudates in the retina without other visible changes to account for their presence.

Once the ophthalmologist's suspicion is aroused, he can confirm the diagnosis by noting the absence of palpable pulsation of the internal carotid artery in the neck, or by measuring the blood pressure in the central artery of the retina with Bailliart's ophthalmodynamometer. Pressure against the side of the globe elicits a visible pulse in the artery over the nerve head. This is a measure of the diastolic pressure there, which is approximately half of the pressure in the brachial artery. More intense pressure on the instrument, to the point of obliterating the visible pulse in the eye, records the systolic pressure. This usually is not useful and most examiners do not elicit it. The instrument is scaled in grams, but the results are so nearly equal to millimeters of mercury that they may be so regarded. A difference of 15 in the readings of the two eyes is significant. Although this instrument has been used in France and some other European countries for 40 years, it has found little favor in this country. In the diagnosis of thrombosis of the internal carotid artery it is frequently helpful. A form of treatment which may prevent thrombosis of the internal carotid artery is long term administration of anticoagulant.

Intermittent Insufficiency of Basilar Arterial System. The syndrome of inter-

mittent insufficiency of the basilar arterial system arises from thrombosis, usually superimposed on an atherosclerotic plaque. Its symptoms indicate transitory impairment of function in the pons, midbrain, or occipital lobes, and may include loss of vision, double vision, ptosis, clouding of consciousness, confusion, hemiplegia, dysarthria, dysphagia, sensory loss in the face or one extremity or half the body, vertigo, tinnitus, vomiting and headache. The symptoms are episodic and may shift from one side of the body to the other. Impairment of vision, when it occurs, characteristically is in the nature of homonymous hemianopsia, indicating involvement of the occipital lobes on both sides with preservation of some visual centers. Complete blindness from insufficiency of the basilar artery is rare. A treatment promising at the present time consists of anticoagulant in the form of Dicumarol administered for a long period—at least several months.

Temporal Arteritis. Temporal arteritis is a disease in which there is inflammation in the walls of the arteries of various parts of the body, especially about the head. It has been termed "cranial arteritis" by some writers, because various deep and superficial arteries of the head in addition to the temporal are implicated; but the necropsies that have been performed in several such cases have shown changes throughout the body; hence the term "cranial arteritis," likewise, is inadequate. By "temporal arteritis" we all know what we mean and the term possesses the virtue of historic priority.

This disease is an occasional cause of the sudden tragic blindness in elderly persons; it occurs with rare exceptions only after the age of 60 years. The temporal arteries become painful, tender, and swollen as a result of inflammation and thrombosis. Other clinical factors include malaise, anorexia, headache, loss of weight, fever, leukocytosis and high sedimentation rate. Intermittent claudication of the muscles of mastication, with pain on chewing, occurs when the deep arteries of the face are involved.

Viewed under the microscope, a section of the temporal artery shows a granulomatous type of reaction involving all the coats, usually greatest in the media. The process extends through the internal elastic layer, disrupting it. Giant cells are present. The lumen of the vessel persists, and thrombosis is not part of this disease. Sections of the artery made after a lapse of several months indicate that the granulation tissue is replaced eventually by scar tissue.

When the arteries of the anterior portion of the optic nerve are involved, as they are in nearly half the cases, loss of vision ensues. Furthermore, when one eye is involved, the chances are greater than 50 per cent that the other eye will become involved also. Vision once lost seldom returns.

Ophthalmoscopically, the common finding is ischemic optic neuritis, with a pale swelling of the head of the optic nerve. In a few cases the involvement of the optic nerve is retrobulbar, and in a few the central retinal artery itself becomes occluded. Wherever the involvement, within a week or two the head of the nerve becomes pale. To the ophthalmologist, temporal arteritis is a medical emergency, because in it the eyes are so frequently involved, and because when one eye is affected the chances are so great that the other will become affected also. The end result may be complete blindness.

The disease runs its course over a period of several months to a year, never

to recur and rarely to cause death. As the cause is not known, treatment is empirical. At present, cortisone acetate is the most effective therapeutic agent, for it seems to control the inflammatory reaction while healing takes place. Early institution of treatment is urgent. While the recommended dosage of cortisone is not standardized, that employed by some of my associates is effective and safe: 300 mg. in divided doses daily for the first few days, gradually reduced to 100 mg. by the end of the first month, then further reduced to a maintenance level of approximately 50 mg. a day in divided doses for the next month or two, and finally tapered off altogether. Knowing when to stop administering the drug is difficult, for the duration of the arteritis is so variable. Vasodilators should not be used. Oxygen administered by mask has been of value during the first few days in some cases. After treatment is started, the general symptoms subside, the sedimentation rate falls, and—what is most important—further loss of vision seldom occurs. But rarely, also, does vision improve.

SUMMARY

Treatment of value, limited though it is, is available for some of the vascular diseases that affect vision, especially among the aged. Hypotensive medication may relieve the spasms superimposed on arterioles in occlusive disease of vessels supplying the eye. Anticoagulants have some efficacy in controlling thrombosis superimposed on occlusion. Cortisone definitely has aided in controlling the visual loss in temporal arteritis. For the control of senile atherosclerosis perhaps nothing will be available until there is more knowledge of the metabolism of lipids and of the aging process.

Comment: Recognition of cerebral arteriosclerosis and an understanding of the various factors involved in thrombosis, ischemia and reflectory arterial spasms are of great importance because the premonitory symptoms, if correctly interpreted, may lead to the appropriate treatment and possible prevention of a major stroke.

The sites of predilection for development of atheromatous plaques and superimposed thrombi are at bifurcations and sharp curves, such as within the carotid siphon from the origin of the ophthalmic artery to the origin of the anterior cerebral artery, in the anterior cerebral artery where it curves over the genu of the corpus callosum, at the first major bifurcation of the middle cerebral artery, at the junction of the vertebral arteries to form the basilar artery, and at the upper bifurcation of the basilar artery.

The small surface vessels are less frequently and severely involved than the large arteries at the base of the brain. Transient ischemic episodes with fleeting phenomena should always be interpreted as incipient thrombosis. In affections of the internal carotid artery, the middle cerebral artery, the basilar arterial system, and the posterior cerebral artery the transient symptoms are often dominated by visual disturbances. Such complaints in older patients should never be ignored even if vision and eye grounds are normal.

In the pathogenesis of carotid thrombosis the concept of an extraneous factor in the form of pressure from the lateral process of the atlas is relatively new When the head is sharply rotated compression of this vessel by the atlantoid process may be demonstrable in arteriograms, causing thrombosis distal to the site of compression. Surgical freeing of the artery from the atlantoid process by adventitial stripping or by amputation of the lateral process may prevent further advancement of the thrombosis.

BERTHA A. KLIEN

ANGIOID STREAKS AND GENERALIZED ARTERIAL DISEASE

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A. M. A. Arch. Ophth., 1957, *57:* 855–868

Histopathologic studies have shown that angioid streaks and pseudoxanthoma elasticum are only part of a generalized elastic tissue degeneration in which the arterial system is included. Further evidence of the close relationship between these anomalies and clinical signs of widespread vascular disease has been obtained from the study of 10 patients, ranging in age from 22 to 63 years. These patients, added to the 24 previously reported on by various workers, constitute a rather significant group already to be found in the literature. There seems to be little doubt that the entity is the result of a generalized degenerative process affecting elastic tissue throughout the body, although the predominant part of the syndrome may be either ocular, cutaneous or vascular.

Symptoms suggestive of vascular disease may be absent, or they may be extreme, depending on the location of the affected vessel and the severity of the involvement. When the arteries of the extremities are affected, the patient may notice paresthesias, numbness, chilling, or intermittent claudication. Objective signs may be obvious or detectable only on careful examination. Pulses may be weak or absent. Pulse waves recorded on an oscillometer are often reduced or even absent. Vasodilatation tests may demonstrate reduced blood flow. Roentgen examination of the extremities often shows calcification of the major arteries. Symptoms may also be produced by involvement of vessels other than those of the extremities.

Detailed general and ocular pathologic studies which were reported in 1938 and 1939 firmly established angioid streaks and pseudoxanthoma elasticum as resting on a basis of generalized elastic tissue degeneration in which the blood vessels often participate. Recognition of the clinical picture of the associated arterial disease was probably stimulated by these pathologic studies. In the present series, all 10 of the patients had angioid streaks of the retina. Macular degeneration, often characteristic of the Junius Kunt type, was present in 8, and the accompanying loss of central vision was the symptom that caused most of the patients to seek medical attention.

Pseudoxanthoma elasticum was also evident in 8 of the patients, one of whom had advanced Paget's disease and another signs suggestive of Paget's disease.

Clinical evidence of arterial disease was present in all of the patients. The most marked involvement was found in the lower limbs, which were affected to some degree in all the patients. The arteries of the arms, on the other hand, were clinically affected in only 6. Pulses were diminished or absent, and arterial occlusion of varying degrees was found. Oscillometric tracings were greatly reduced. X-rays of the extremities demonstrated calcification in many of the

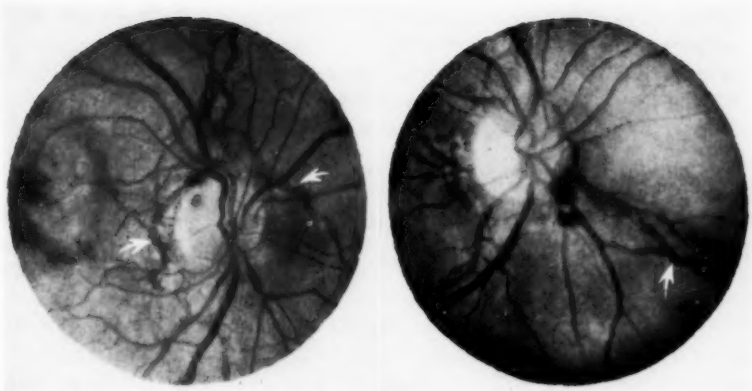

FIGURE 1. Fundus photographs showing typical angioid streaks, right and left eyes. (Courtesy of Scheie, H. G., and Hogan, T. F.: A. M. A. Arch. Ophth., 1957, *57:* 855–868.)

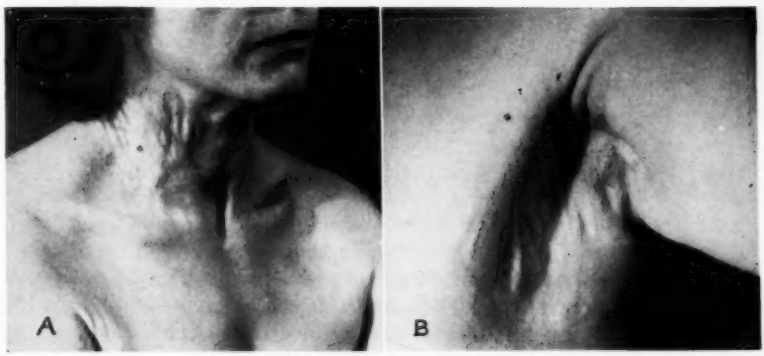

FIGURE 2. Photographs showing typical changes of pseudoxanthoma elasticum. *A*, about the neck; *B*, axilla. (Courtesy of Scheie, H. G., and Hogan, T. F.: A. M. A. Arch. Ophth., 1957, *57:* 855–868.)

arteries of medium and larger size. Intermittent claudication was a common complaint. The existence of such advanced vascular disease in comparatively youthful patients was striking.

Evidence of cardiac disease and myocardial damage was found in 3 patients. One patient had an aneurysm of the internal carotid artery. Another had an aneurysm of each common carotid artery. Calcification was found in the walls of the aneurysms. Another patient showed calcification of the choroid plexus of the brain, and still another, calcification of the internal carotid artery. One patient was found to have bilateral calcification of the renal arteries as well as of the celiac axis.

The mechanism underlying the degenerative process responsible for this entity is obscure. No disturbance in metabolism has been demonstrated, nor has it

been possible to detect a hereditary element that might account for the generalized degeneration in the elastic tissue.

Since any part of the clinical picture may predominate, or even occur alone, patients with obscure arterial disease, especially of an occlusive character, should be given a careful physical examination with this condition in mind.

Comment: Whenever confronted with one of the triad of findings consisting of angioid streaks, pseudoxanthoma elasticum and arterial disease of unexplained origin, reemphasized in this publication, it should be obligatory to search fo evidence of the other two.

The fact that these three manifestations of a unique systemic involvement of the elastic tissue of the body belong to three different specialties of medicine does not make it easy to keep this unity in mind at all times.

BERTHA A. KLIEN

Therapeutics

TREATMENT OF EROSIONS OF THE EYE CAUSED BY LIME

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Klin. Monatsbl. Augenh., 1957, *130:* 536–539

For a long time the early transplantation of the mucosa of the lips was considered the method of choice for treatment of severe erosions of the eye, but in the course of recent years new drugs have become available which make surgical intervention unnecessary, provided these drugs are administered early and in adequate amounts. Many authors have reported their experiences (Meyer-Ratken, Thiel, Haselmann, Pulfrich, Leydhecker, and others) and these reports give a clear picture of the results of the conservative medicinal treatment of erosions of the eye. Haselmann reported favorable results of treatment of erosions caused by lime, acids and lye, with an acetylcholine-chloride-choline ointment which has a prolonged effect. Acetylcholine drops have the disadvantage that they are rapidly destroyed and, therefore, repeated application at short intervals is required (Haselmann and Pulfrich). Many authors (Zwahlen, Fanta, Jaensch, Budde, Friede, Nagy, Thiel and Franceschetti) recommended Priscol. Leydhecker advised treatment of erosions of the eye with 1-(4-oxyphenyl)-1-oxy-2-*n*-butylamino-ethane-sulfate (Vasculat). Fischer, Hodgson, Wagenaar and Goldmann treated erosions successfully with Sympatol (*p*-methyl-amino-ethanol-phenol tartrate).

Lohlein and Gasteiger cautioned against the original Denig's procedure because of the transplantation of the cornea which occasionally may be necessary

later on. Gasteiger changed completely to conservative treatment in the course of recent years. Also Passow and Comberg recommended early transplantation only for severe erosions. In all the other cases, the perilimbal undermining of the conjunctiva bulbi corresponding with the spread of the chemosis, as described by Passow, has proved effective by causing the draining of the toxic transudate, thus being the decisive step in healing.

In the author's own experience 88 patients with erosions of varied degree caused by lime were treated at the ophthalmologic clinic in the course of the last few years. According to symptoms the patients were subdivided in three groups:

Group I consisted of patients with mild erosions associated with fine stippling of the cornea and conjunctival congestion. Of 20 patients in this group 8 were hospitalized and 12 were ambulant. After conservative treatment for only 3 days all patients had full vision. There was not a single complication. Opaque scars did not occur in the cornea of any of the patients and there was no formation of symblepharon.

Group II consisted of 36 patients with erosions associated with chemosis and with erosion or vesiculation of the cornea. All the patients were hospitalized for from 1 to 4 weeks. Healing without complication and with full vision resulted from medicinal treatment in 35 patients. One patient had to be discharged after 8 days of treatment with vision being improved from 4/35 to 4/15. A central, fine corneal scar was present.

Group III consisted of 32 patients with erosions with signs of ischemia and extensive necrosis of the conjunctiva and with parenchymal opacities of the cornea. Of the 32 patients 22 were given conservative treatment and 10 were operated upon. The choice between conservative and surgical treatment did not depend on the severity of the erosion. Transplantations of the mucosa of the lips were performed only up to 1952. Since then even the most severe erosions caused by lime were treated conservatively.

Of the 10 patients operated upon, 4 obtained full vision without complications within 4 to 6 weeks after the transplantation of the mucosa. Permanent opaque scars occurred in the cornea of 6 patients with a change in vision of from 4/25 to 4/10; 4/50 to 4/8; 2/50 to 4/10; and 4/35 to 1/35; movements of hand to 4/50. Symblepharon formation could not be avoided in 2 patients.

Of the 22 patients treated conservatively, 19 were discharged from hospital after a course of healing of from 1 to 5 weeks without complications and had obtained full vision. Of the remaining 3 patients, 2 did not reach full visual capacity because of residual scars in the cornea, but one of the patients obtained improvement of vision from 2/50 to 4/20, and the other from 4/50 to 4/8. Very fine symblepharon formation remained in the lower conjunctival fold in the third patient. Lime particles had been present in the conjunctival sac for many hours before the institution of treatment.

In the conservatively treated patients an attempt was made to obtain maximum dilatation of the conjunctival and deeper vessels with the aid of the drugs after careful cleansing of the conjunctival sac and particularly of the conjunctival

folds. Depending on the individual patient, various drugs in various doses were used. At the start of the treatment and according to the need in the course of the following days, priscol (in solution 0.01 gm. per 1 cc.) was injected into the conjunctiva once or several times daily after local anesthesia, particularly in the erosion area. It is important that the eroded conjunctiva, which has become compounded with its base, can be loosened again with the aid of the subconjunctival injection. Care must be taken that the "Priscol cushion" be pushed forward to the limbus. This is a very important feature of the conservative treatment, because thus an immediate blood perfusion of the conjunctival vessels and particularly of the marginal loops is obtained in the acute stage, and the regenerative tendency of the cornea receives decisive support. A special attempt was made to maintain this "Priscol cushion" by one or several daily injections depending on the individual situation. Likewise, from the start of treatment, a Priscol-sulfamethazine (Elkosin)-polysorbate (Tween) ointment (10 per cent sulfamethazine, 5 per cent priscol and 5 per cent Tween) was applied locally up to five times daily and the eye was covered with a dressing; in case of severe erosion, homatropine or atropine and heat were applied. The Priscol-sulfamethazine-Tween ointment (which according to information supplied by Ciba is not yet available on the market) has been described as highly effective by Reiser and Vorlaender. Several patients with erosions caused by lime were given, in addition to priscol injections (after normalization of the blood perfusion of the conjunctiva), Arovit eye ointment (100.000 I.U. of vitamin A per gm. in the form of vitamin A palmitate, and as ointment base a mixture of Vaseline and whale fat); this ointment was applied up to eight times daily. It had a good effect on epithelial regeneration and clearing of corneal opacities. The favorable effect of this ointment was observed also in burns, erosions and ulcers of the cornea and on corneal dystrophy. Animal experiments with Arovit ointment applied to artificially produced corneal erosions gave negative results as reported by Nover, Ullerich and Durchschlag.

Pantobenzyl (Dispersa eye ointment) exerted a satisfactory effect on epithelial regeneration and improved the blood perfusion of ischemic or anemic conjunctival areas. This preparation contains calcium pantothenate, which favors epithelial regeneration, and benzylimidazoline, which exerts a vasodilator effect.

Comment: Strictly speaking, the injuries the author describes are due to quicklime (calcium hydroxide) rather than to lime (calcium oxide). This is not mere quibbling since it is the hydroxyl ion that is responsible for the caustic action rather than the calcium ion. (Calcium chloride, for example, is innocuous to the eye.) However lime is quickly hydrated on contact with the moist globe and furthermore the term "lime burn" is well established historically.

The author condemns the Denig graft (removal of all burned conjunctiva and replacement by oral mucous membrane). It is true that this treatment is unnecessary in mild injuries but it may be eye-saving in severe total burns of the globe. He recommends instead the subconjunctival injection of vasodilators such as 2-benzyl-2-imidazoline HCl (Priscol). There is little experimental or clinical evidence to prove that ischemia of the conjunctiva is responsible for the eventual destruction of the cornea that occurs in some

cases. Furthermore if the injury were severe enough to obliterate the conjunctival vessels there would in effect be nothing to dilate.

The secret of the author's successful nonsurgical treatment is probably "most careful cleansing . . . of the conjunctival sac and particularly of the conjunctival folds." In addition a sulfonamide preparation and a bland vitamin A ointment were instilled frequently. These added variables make evaluation of the author's results difficult. Ideally one should compare two series of cases with burns of equal severity and with similar therapy except for the drug under investigation. This is obviously a difficult clinical problem but should present no insurmountable obstacles to the avid experimenter in the small animal laboratory.

DAVID SHOCH

TREATMENT OF RETINAL ARTERY OCCLUSIONS

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Am. J. Ophth., 1957, *43:* 947–951

Arterial spasm is probably present in every case of occlusion from whatever cause. Certainly arterial spasm follows closure of a vessel by a thrombus or an embolus or any other agent that leads to blockage of the lumen. On the other hand, there does not seem to be any valid reason for assuming that spasm must necessarily follow a vascular accident; it could just as well occur independently of any thrombosis or embolism or other injury to the vessel. Why spasm should occur independently, however, cannot be stated any more than it can in Raynaud's disease. Clinically, as a rule, no other pathologic lesion can be discovered, although it was noticed in one series of cases that most of the patients were less than 40 years of age. In addition, most of these patients gave a history of "cold fingers," that is, there was usually some evidence of peripheral vascular instability, perhaps from some sympathetic-parasympathetic imbalance. Frequent remissions were also reported. In this group, arterial spasm was obviously the principal if not the sole factor responsible for the occlusion.

Another broad group in which retinal artery occlusion occurs consists of patients who are past middle life and who are arteriosclerotic or hypertensive or both, and whose general background is, therefore, favorable to a vascular accident such as thrombosis.

If the premise that arterial spasm is a factor in the production of retinal occlusion is accepted, it follows that treatment must be directed toward relieving the spasm. Vasodilators must be used intensively and immediately. Patients with arterial thrombosis will be benefited by the use of anticoagulants in addition to vasodilators. Experience seems to show that any vasodilating agent will be effective, provided there are no contraindications to its use and provided it is

given early enough. Retrobulbar injection, which enables the drugs to act directly on the sympathetic nerve endings in the smooth muscle of the arteries and arterioles, is the best method of administration for immediate treatment, but oral administration should be used as a supplementary measure. Treatment with Priscol, which is quite effective but which is contraindicated in coronary disease and peptic ulcer because of its histamine-like action and which must be used with care in diabetes, or with Ronicol which, though rather more painful than Priscol, is just as harmless and is unquestionably effective, was successful in bringing about the restoration of useful vision in several of 17 patients reported by the author. The first 3 of these cases were described in detail in an earlier article.

Comment: The author urges the acceptance of the premise that prolonged reflex spasm is a factor in the production or at least in the persistence of retinal arterial occlusion regardless of its pathogenesis. Therapy should always include antispasmodics given as promptly as possible in the combined oral and retrobulbar routes. The author seems to prefer the painless imidazoline hydrochloride (Priscoline) to the alcohol of nicotinic acid (Ronicol) for retrobulbar injection. He does not mention the individual dose or frequency of administration, but 1 cc. of Priscoline (25 mg.) is the customary dose which may be given daily or even twice a day. Its main contraindications because of its histamine-like action are coronary artery disease and peptic ulcer.

In his series of 17 cases, ranging in ages from 19 to 80 years, the author had uniformly good results with this treatment in persons below the age of 43. In only 3 patients of this age group was the vision not restored to normal, but in all 3 therapy was started from 10 to 30 days after the loss of vision. The shortness of the interval between onset of the occlusion and initiation of therapy proved to be even more important in the older age groups.

In patients above the age of 40 or 45 with the possibility of an arteriosclerotic factor in the occlusive mechanism, additional therapeutic measures should be considered. The recently suggested treatment of sclerotic arterial occlusions with heparin as a lipolytic clearing factor might be a good choice (H. Stark: Klin. Monatsbl. Augenh., 1957, *130:* 72). Treatment with heparin may be conducted in such a way that at first its anticoagulant and fibrinolytic action is utilized by administration of higher dosages for several days (50,000 units intravenously daily), followed by daily intravenous injections of 6000 units for a period of 15 to 20 days.

It has been pointed out that the effectiveness of heparin in reopening sclerotic arterial occlusions may result in a temporary increase of retinal edema and even in hemorrhages, which exudative phase disappears, however, on continuation of the therapy.

The general contraindications to the administration of low doses of heparin continued over a prolonged period are advanced age over 70 years, pregnancy, renal hypertension including the late complications of diabetes mellitus, the history of peptic ulcer, and extensive varicose veins with or without phlebothrombosis.

BERTHA A. KLIEN

USE AND MISUSE OF ACETAZOLEAMIDE (DIAMOX) IN THE TREATMENT OF GLAUCOMA

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A. M. A. Arch. Ophth., 1957, *57:* 639–643

The discovery that the carbonic anhydrase inhibiting drug acetazoleamide (Diamox) brings about a lowering of the intraocular pressure has caused it to be used in the treatment of glaucoma. Its pressure lowering effect, however, is due solely to a lessening of the rate of aqueous production while the obstruction to the outflow of aqueous remains unchanged. Treatment with Diamox must therefore be regarded as a palliative measure, but one that is often of tremendous value in preventing damage to vision while efforts are being made to relieve the fundamental difficulty, which is the obstruction.

New and valuable additions to the therapeutic armamentarium are usually hailed with enthusiasm, but unfortunately this very enthusiasm often leads to their unwise use, especially at first. This was true of the sulfonamides and antibiotics and of the steroids. Similarly, it is becoming increasingly apparent that an unwise use is being made of Diamox in the treatment of some forms of glaucoma. Its greatest usefulness is in the treatment of secondary glaucoma which, by definition, is a rise in ocular tension secondary to some other eye disease. If the fundamental disease can be cured, the secondary glaucoma is likewise cured. Formerly, palliative surgical procedures were often used in cases of secondary glaucoma to prevent serious damage to vision from the increased tension while the disease was running its course, but now acetalozeamide serves the same purpose and has proved to be of inestimable value.

In open angle glaucoma, the obstruction to outflow which results in increased ocular tension resides somewhere in the filtration apparatus. This form of glaucoma is treated by miotics and, when necessary, by various filtering operations designed to increase drainage from the anterior chamber. Likewise, acetazoleamide, if tolerated by the patient, may be used at any stage of open angle glaucoma. Its pressure lowering effect as an adjunct to miotic therapy may protect the eye from damage so that in some cases operation can be avoided. Moreover, the use of acetazolamide has no deleterious effect on the disease itself, nor does it lessen the effectiveness of any other form of therapy, either medical or surgical. Thus in open angle glaucoma nothing contraindicates its use except the unpleasant side effects experienced by some patients.

In angle closure glaucoma, on the other hand, the situation is quite different. Here the obstruction to outflow is due solely to closure of the angle. The outflow channels, at least in the early stages of the disease, are completely normal and the tension rises and falls as the angle closes and opens either spontaneously or under the influence of miotics. The level of the tension is a fairly accurate guide

to the extent to which the angle is closed at a given time. If the tension is normal, either spontaneously or as a result of miotics, it may be assumed that the angle is completely or nearly open. Gonioscopy confirms this assumption. Now, if the tension remains elevated in angle closure glaucoma so that the angle is closed, the closure may be made permanent by the formation of peripheral anterior synechias. Though the tendency to the formation of permanent peripheral anterior synechias varies greatly in different eyes, it is an ever present danger. Treatment of angle closure glaucoma of whatever type is therefore predominantly surgical. In an early case, when there are only a few or even no peripheral anterior synechias, peripheral iridectomy effects a complete and permanent cure. Later, when a considerable portion of the angle is permanently closed by synechias, a filtering operation is required and in these neglected cases all operations may fail and the eye may be lost. This, then, is a form of glaucoma in which in the early stages a simple surgical procedure effects a complete cure, and in the late stages all treatment may fail.

Unfortunately, if acetazoleamide is used with miotics in the treatment of angle closure glaucoma, the level of the tension no longer serves as a guide to the extent to which the angle is closed. When acetazoleamide is used, the tension usually falls to the normal range, creating a false sense of security, while the angle may remain closed. If the treatment is continued and the angle becomes permanently closed by synechias, the chance for simple peripheral iridectomy has been lost and a filtering operation, which is not only more hazardous but also less certain to succeed, will have to be undertaken.

On the other hand, once operation has been decided on in angle closure glaucoma, acetazoleamide is a valuable adjunct to therapy because it reduces tension and thus lessens the operative risk. After operation for angle closure glaucoma, either iridectomy or a filtering procedure, there may be a certain amount of residual glaucoma. In many cases, this residual glaucoma can be controlled by medical means and acetazoleamide will be found useful for this purpose. It is not contraindicated and may be used freely, since no further closure of the angle is to be expected and there is, therefore, no danger of masking danger signs and symptoms.

Comment: Chandler's comments on the use of Diamox are very timely and important. They will be applicable to any of the newer drugs which will become available in the treatment of glaucoma. Drugs like Diamox which decrease the rate of aqueous formation and thereby lower tension may lull the doctor and the patient with angle closure glaucoma into a false sense of security, as Chandler indicates. The indications which he gives are certainly correct. The only problem arises in those cases where the angle closure mechanism is acting but where the absence of congestion leads to a false diagnosis in spite of a shallow anterior chamber. Such cases, fortunately, are relatively infrequent but they do occur. Evidently mild congestive episodes occur in some cases without the patient being aware of them, but peripheral anterior synechias do form, nevertheless. Failure to use gonioscopy for help in diagnosis may be responsible for some of these failures.

H. Saul Sugar

Systemic Disease

DIABETIC OPHTHALMOPLEGIA

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A. M. A. Arch. Neurol. & Psychiat., 1957, *77:* 337–349

Paralysis of the third, fourth, or sixth cranial nerve as a complication of diabetes was first recognized as a clinical entity by Ogle in 1866. Since that time numerous detailed clinical descriptions of cases of ocular palsy in diabetic patients have appeared in the medical literature. As many writers have observed, the ophthalmoplegia is often seen in patients who have had mild diabetes of long standing, frequently complicated by retinopathy, nephropathy, peripheral neuropathy, and lenticular opacities. The third and sixth cranial nerves are the ones most frequently affected, the paralysis coming on rapidly, sometimes in a matter of hours, and clearing up completely within a few weeks or months. The ophthalmoplegia is frequently accompanied by pain, often severe, which is localized within or behind the orbit in a distribution which may correspond to the ophthalmic division of the trigeminal nerve. When the third nerve is affected, pupillary function often remains undisturbed. One or both eyes may be affected, usually in succession.

The pathology of this condition, which has never hitherto been reported, has remained a subject of much speculation. A metabolic lesion, inflammation, or arterial disease with ischemic degeneration of the nerve, an infarction or hemorrhage in the nucleus or in the intramedullary parts of the nerve have all been postulated at one time or other.

A case of oculomotor nerve palsy occuring in a 62-year-old diabetic woman who died five weeks following the onset of her illness as a result of carotid arteriography is reported. This case report contains the first description of the morbid anatomy of diabetic ophthalmoplegia. Although it failed to provide a complete solution to its cause and pathogenesis, it does account for many of the puzzling features of the disease.

This case presented a number of interesting clinical, anatomic, and pathologic features which deserve further comment. The paralysis of the ocular muscles supplied by the oculomotor nerve was remarkably complete, more so than one would have expected from observing the extent of the lesion. As a rough estimate not more than one fourth or one fifth of the nerve fibers had disappeared or was in the process of degeneration; yet all the oculomotor functions except pupillary constriction, and probably ciliary muscle action, had been paralyzed

for more than five weeks. Paralysis was to a large extent due to a disorder of function rather than an irreversible structural change.

The retention of pupilloconstrictor function probably had as its anatomic basis the sparing of nerve fibers in the peripheral or subepineurial part of the nerve. Many of these peripheral fibers are of small diameter, and Hughes has observed that the oculomotor nerve is the only one of the ocular nerves which contains a large percentage of small fibers in its periphery. Apparently the superficial position of these fine fibers both exposes them to external pressure and protects them against the effects of ischemia.

The pathologic process was remarkable in several respects. First, it had induced a fusiform enlargement of the oculomotor nerve, which on microscopic section proved to be a mixed pseudoneuroma and neuroma. For a distance of 1 cm. the nerve was swollen to 1½ times its normal diameter. This enlargement was not due solely to a proliferation of axons and connective tissue from the proximal end of the lesion, like an ordinary traumatic neuroma, but was the result of edema and cellular infiltration, as well as an increase in connective tissue in the endoneurium, perineurium, and epineurium. In certain respects the lesion resembled the pseudoneuroma described by Tinel and others in their studies of nerve injuries. Both Denny-Brown and Brenner have shown that there is a constantly changing microscopic pathology in pseudoneuroma. Beginning as a congestion of blood vessels, edema, and a segmental shattering of myelin sheaths, it continues for some weeks as a cellular infiltration and an edema of the interstitial tissue. Finally it subsides unless some of the nerve fibers have been interrupted, in which case fibrosis and axonal proliferation add to the volume of the injured segment. In the latter instance a pseudoneuroma becomes a neuroma. Presumably this took place here.

The principal characteristic of the microscopic lesion was an incomplete necrosis of parenchymal and interstitial tissue. All neural elements—myelin sheaths, axis cylinders, Schwann cells and connective tissue—were affected in the region of maximum damage: connective tissue and axons of the central stump had begun to proliferate. The changes in the oculomotor nucleus were assumed to be of secondary type, whereas those in the segment distal to the lesion were typical of Wallerian degeneration. Other noteworthy features of the phonologic process were overgrowth of connective tissue involving epineurium, perineurium and, to an even greater degree, the endoneurium: an arteriosclerosis of the intraneural vessels, with a fibrinoid change in one of them, and a regeneration of axis cylinders.

These pathologic changes could be best explained as direct effect of and reaction to an incomplete focal ischemia resulting from occlusion of a nutrient artery. However, no occluded artery or vein was found either within or on the surface of the nerve in serial sections through its entire length. Nor could any demonstration be made of relationship between the lesion and the curious deposits of material which characterize Kimmelstiel-Wilson disease and the vascular changes in diabetic retinopathy. It is possible that a nutrient artery had become thrombosed at its origin from a larger artery outside the nerve, and that it had been overlooked

in the postmortem examination because of ignorance of the arterial supply of the oculomotor nerve. The demonstration of fairly severe vascular disease elsewhere would favor this explanation, and it also has the support of other studies of diabetic neuropathy such as that of Woltman. Moreover, the lesion itself bore a striking resemblance to what has been called "ischemic neuropathy."

The lesion in this case is also similar in certain respects to those seen in periarteritis nodosa, another example of an ischemic neuropathy. Kernohan and Woltman found, in their cases, areas of infarction in sciatic nerves and a marked increase in connective tissue.

These impressions of the changes that seem indicative of ischemia seemed to be shared by Krueke, who felt that Wallerian degeneration and fibrosis were common denominators of the ischemic neuropathies. The sudden or acute onset and steplike progression of the ophthalmoplegia in this case, and in others very similar to it, would be best accounted for on the basis of ischemia.

In order to clarify the possibility of vascular occlusion and ischemic neuropathy of a cranial nerve, a series of dissections was carried out in human beings and animals, showing that the oculomotor nerve is supplied by vessels which lie in close proximity to it. In order to determine the exact origin of the major nutrient vessels which supply the various portions of the oculomotor nerve, a red colored Neoprene was injected into the basilar and internal carotid arteries. This demonstrated the blood supply of the trunk and the intraorbital part of the oculomotor nerve.

However, it was most difficult to determine the vascular supply of the cavernous portion of the oculomotor nerve within the cavernous sinus. Despite the close proximity of the third nerve to the internal carotid artery siphon, no vessel could be traced from its wall to the third, fourth or sixth nerves.

Since the exact vascular pattern of the case under discussion is not known, one can only postulate that the nutrient artery supplying the anterior cavernous portion of the left oculomotor nerve may have carried an important part of the blood supply to this nerve. If this vessel had become occluded by thrombosis at a site prior to entering the nerve, infarct necrosis could have occurred in the distal intracavernous portion of the third nerve.

This case established at least that some instances of diabetic ophthalmoplegia are probably due to lesions in the orbital or retroorbital parts of the affected nerve. There was, however, failure to identify the nature or exact site of the lesion or to prove its specific relationship to diabetes mellitus.

Comment: It is strange that diabetic neuropathy as a cause of extraocular muscle paralysis is so poorly documented in the ophthalmic literature. All authorities agree that there is an absolute increase in the number of diabetics in the population as a whole. It should not therefore be surprising that complications are encountered more and more frequently, and one of these complications is diabetic neuropathy involving the third, fourth or sixth cranial nerve.

Clinically, this is characterized by the rapid onset of a diplopia, depending on the muscle or muscles involved, and the ultimate spontaneous improvement when the diabetes is controlled. The pathology of the involved nerve trunk has not heretofore been

explained adequately. Woltman and Wilder felt that occlusive vascular phenomena were responsible for the findings and symptoms. The pathology described in this case of diabetic neuropathy of the oculomotor nerve tends to substantiate this theory, and yet it is difficult to reconcile the usual complete clinical recovery with the picture described. The authors try to explain this discrepancy by the fact that there is complete destruction of only a fraction of the axis cylinders, but this is not an entirely convincing argument.

As a by-product of this pathologic study, the authors did much investigation of the blood supply of the oculomotor nerve which has never previously been worked out. They encountered numerous technical difficulties which they were not able to overcome entirely.

From a clinical standpoint, it is important that all cases of extraocular muscle paralysis of rapid or sudden onset be investigated for a possible diabetes mellitus. If this is found, it is important to remember that the prognosis is good in the great majority of patients and that there need be no treatment other than adequate control of the diabetes.

DANIEL SNYDACKER

FACTORS IN THE PATHOGENESIS OF DIABETIC RETINOPATHY

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Tr. Canad. Ophth. Soc., 1956, *8:* 122–135

The factors involved in the pathogenesis of the degenerative complications of diabetes have been studied by various groups in many different ways over the years. In 1952 a new approach to the problem was outlined by Becker when he suggested that one of the basic differences between the diabetic patient with retinopathy and the diabetic patient without retinopathy may lie in the functional capacity of the adrenal cortex. Four lines of evidence—clinical, histopathologic, investigative, and experimental—were brought forward when Becker first considered the possibility of relative adrenal cortical hyperfunction in diabetics with retinopathy, and the studies that have since been made can be grouped under the same headings.

The clinical evidence so far obtained includes (1) the appearance of capillary aneurysms in nondiabetic patients who were being given corticotropin or cortisone for various reasons, and the disappearance of the aneurysms in some cases when the adrenal cortical hormone was withdrawn; (2) the appearance of diabetic diabetic retinopathy in nonhypertensive diabetic patients during pregnancy and its disappearance after delivery; (3) the disappearance of advanced diabetic retinopathy in a patient in whom Simmonds' disease developed after delivery; (4) stabilization, improvement, or disappearance of retinopathy in various patients after hypophysectomy or adrenalectomy; and (5) improvement, re-

ported by some authors, in diabetic retinopathy after the administration of testosterone.

Among the histopathologic findings, particular interest attaches to reports by Friedenwald and by Ashton that the incidence of Kimmelstiel-Wilson nephropathy in diabetic patients with retinal disease is 58 per cent and to the fact that neither of these authors found a single instance in which kidney lesions of this kind were observed without histologic evidence of retinopathy. A clearcut difference has also been found to exist between diabetic patients with Kimmelstiel-Wilson lesions and those without such lesions in respect to the average weight of the adrenal glands, which was greater in the patients with kidney lesions, and to the existence of vacuolization in the zona fasciculata of the adrenal cortex, which was present in 86 per cent of 64 patients with Kimmelstiel-Wilson lesions but in only 12 per cent of 91 patients without such lesions. Moreover, the incidence of adrenal cortical adenomas in patients with nephropathy was 14 per cent, while in patients without nephropathy it was only 3.3 per cent. Another significant histopathologic finding was the postmortem discovery of kidney lesions similar to those of Kimmelstiel-Wilson disease in patients who had received massive doses of cortisone. One of these patients could not be proved to be a diabetic by ordinary laboratory criteria, but it may be significant that he had a family history of diabetes.

Investigative evidence consists principally of the findings (1) that urinary excretion of 17-ketosteroids is significantly higher in diabetic patients with retinopathy than it is in those without retinopathy; (2) that the administration of cortisone by mouth to 16 patients with retinopathy was followed within 4 hours by a drop in the number of circulating eosinophils amounting to 50 per cent or more, whereas such a drop occurred in only 3 of 19 patients without retinopathy who were given a similar dose of cortisone; and (3) that patients with retinopathy handle vitamin B_{12} in a manner differing from that of patients without retinopathy and resembling that induced by the administration of cortisone.

In the experimental field, kidney lesions with a superficial morphologic resemblance to those of Kimmelstiel-Wilson disease have been produced in rabbits by the use of adrenal steroids and of corticotropin. Even when the adrenal steroids are given in massive doses, however, it has not yet been possible to produce capillary aneurysms in the retinas of experimental animals, and this fact constitutes one of the principal weaknesses of the theory which attributes diabetic retinopathy to hyperfunction of the adrenal cortex. In judging the efficacy of any treatment such as adrenalectomy or hypophysectomy which is based on this approach to the problem of diabetic retinopathy, it must be remembered that the disease is characterized in its normal course by remissions and exacerbations and that any improvement apparently due to therapy may in fact have come about spontaneously. As a working hypothesis, however, the theory, which is largely consistent with the available evidence, provides an excellent starting point for various avenues of research.

THE ADRENAL CORTEX AND DIABETIC RETINOPATHY

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Tr. Canad. Ophth. Soc., 1956, *8:* 156–169

There is still a great deal of controversy about the relationship of retinal disease to the degree of control of blood sugar, but it is now generally accepted that the most important element in the relationship is the duration of the diabetes. The histopathologic picture of diabetic retinal disease has been well defined, and histochemical studies on the retina and kidney of diabetic patients have shown a striking similarity in the staining characteristics of the Kimmelstiel-Wilson renal lesions and the microaneurysms that occur so abundantly in diabetic retinopathy. At least 80 per cent of patients with diabetic glomerulosclerosis have been shown to have ophthalmoscopic evidence of retinopathy, and an even higher correlation has been found at postmortem examination. Kimmelstiel-Wilson glomerulosclerosis and diabetic retinopathy are both specific vascular lesions occurring in diabetes mellitus and it seems possible that they have a common histogenesis. The suggestion has been made that a relative hyperactivity of the adrenal cortex may be implicated in the development of these lesions and experimental, clinical, and histopathologic evidence has been accumulating which tends to support this hypothesis.

A comparative study was therefore made of the 24-hour urinary 17-hydroxycorticosteroid excretion of three groups of persons. Group I consisted of 39 normal individuals drawn from hospital personnel. Groups II and III consisted of diabetic patients drawn from the outpatient services of the Diabetic Clinic, Johns Hopkins Hospital. These patients were carefully examined under mydriasis (1 per cent Cyclogyl, 10 per cent Neo-Synephrine) and were classified ophthalmoscopically as retinopaths or nonretinopaths. The degree of retinopathy varied in severity from one or two microaneurysms to retinitis proliferans. Group II consisted of 47 nonretinopaths and Group III of 49 retinopaths.

The results of the study, which are shown in Table 1, provide neither a contradiction to nor definite proof of the adrenal cortical hypothesis. Although the daily 17-hydroxycorticosteroid excretion fluctuated widely among individuals, no significant difference in excretion values was found when either of the two diabetic groups was compared with the normal controls. Diabetic patients with retinopathy, however, have a significantly higher excretion than have those without retinopathy. Moreover, diabetics as a whole excrete a significantly smaller fraction of an oral test dose of compound F than do normal controls. Consequently, the increased 17-hydroxycorticosteroid excretion by the retinopaths may be attributable to an increased production of compound F by the adrenal gland. The difficulties of evaluating glandular function, especially in a gland with such a complicated functional capacity as the adrenal, by the use of

TABLE 1

Comparison of 24-Hour Urinary Excretion of 17-OH-CS by Normal Patients and Diabetics with and without Retinopathy

	Normals		Diabetics			
			Without retinoppathy		With retinopathy	
	Female	Male	Female	Male	Female	Male
Number of cases	16	23	28	19	32	17
Age range	20–66	17–84	32–73	27–74	35–73	36–76
Range (mgs. 17-OH-CS)	2.3–6.9	2.2–10.2	1.5–9.3	0.8–8.9	1.8–13.5	3.3–13.2
Mean 1 (mgs. 17-OH-CS)	4.7	6.5	5.2	4.7	6.4	6.6

urinary excretion studies make it impossible at present to determine whether, or how, it contributes to the vascular pathology so characteristic of diabetes mellitus.

The possibility that one of the ways in which the renal and retinal lesions in diabetes are produced may be a disturbance of mucoid metabolism induced by the diabetes and exacerbated by adrenal cortical hyperfunction was investigated in a second set of studies. The serum mucopolysaccharides are to be found in the globulin fractions, with about 75 per cent in the α-2-globulin and 25 per cent in the α-1-globulin. Diabetic patients with retinopathy were found to have a significantly elevated serum α-2-globulin level. In diabetic patients without retinopathy, on the other hand, the α-2-globulin level was the same as that in normal controls.

Experimental findings in diabetic rabbits given a 3-week course of cortisone injections revealed a significant elevation in the serum α-2-globulin levels Renal lesions of the Kimmelstiel-Wilson type developed in at least 80 per cent of these rabbits.

Study of the serum glucosamine levels showed them to be elevated in all the diabetic patients, but no statistically significant difference was discernible between the levels in the diabetic patients with retinopathy and those in the patients without retinopathy. A slight but not significant elevation in serum glucosamine levels appeared in the alloxan diabetic rabbits after a 3-week course of intramuscularly administered cortisone.

It has recently been shown by the use of labeled glucose that the animal cell is capable of synthesizing its own glucosamine from glucose, and that it has the means for N-acetylation and phosphorylation as well. These may indeed be the preliminary stages in the synthesis of the mucosubstances. Glucosamine or its precursors, or both, are probably formed in the liver and transported to the other tissues for incorporation into the mucoids. Since the liver appears to be the most active center for carbohydrate metabolism in the body, it may be the place where the effect of diabetes on mucoid metabolism becomes apparent. It may be postulated that the effects of hormonal imbalance on mucoid metabolism in the diabetic state will eventually appear in the form of diabetic retinopathy and intercapillary glomerulosclerosis.

Comment: Diabetic retinopathy remains one of the outstanding problems demanding concerted research efforts. Its increasing incidence, particularly in the young diabetic kept alive by insulin, presents one of the most distressing problems facing the ophthalmologist as well as the endocrinologist.

A possible role of the adrenal cortex in the pathogenesis of diabetic retinopathy and Kimmelstiel-Wilson nephropathy was suggested in 1950. Since the formulation of the original hypothesis and the review of accumulated supporting data in 1954, several contributions and observations have been made which are consistent with the adrenocortical hypothesis. Unfortunately none of these suggestive findings has offered conclusive proof that the adrenal cortex plays a causative role in the production of retinopathy and nephropathy. However, whether the role be direct or permissive, there is a remarkable amount of data implicating the adrenal cortex in these complications of diabetes.

In the first of there papers, the basis of the original hypothesis is reviewed by Rosen and brought up to date with data collected from the literature as well as the laboratory. The alleged arrest of retinopathy in hypophysectomized and adrenalectomized patients is discussed as evidence for the thesis. Rosen properly advises caution in accepting the tentative working hypothesis of abnormal adrenocortical function as a basis for radical therapy. He further draws attention to the variable rate of progression of the disease process and consequent difficulty in drawing conclusions from therapeutic attempts.

In the second paper, Lerman quotes the data on the increased steroid excretion in diabetic patients with retinopathy as compared to the nonretinopathy group. However, the existence of differences in steroid output by diabetics with and without retinopathy have been questioned recently by Rifkin and Lieberman (Seventeenth Annual Meeting, American Diabetes Association, New York, June 1957). In fact these workers failed to find any significant differences in adrenal cortical activity in diabetics with and without degenerative changes as judged by blood and urinary steroid levels as well as the effects of adrenocorticotropin hormone (ACTH) stimulation. Part of the discrepancies in results reported from various laboratories may stem from the different criteria used in the diagnosis of retinopathy.

The finding of Lerman of a statistically significant elevation in serum α-2-globulin in diabetics with retinopathy confirms earlier work along these lines. Most exciting is his finding that in the alloxan diabetic rabbit, cortisone induces a significant rise in α-2-globulin. These findings provide further suggestive evidence for the similarity of the cortisone induced experimental lesion in the rabbit and the Kimmelstiel-Wilson lesion in the diabetic patient. Similar evidence has become available in cortisone treated patients. Thus, Sommers and Haley (Proc. Soc. Exper. Biol. & Med., 1956, *91:* 263) have reported finding in the glomeruli of nondiabetic patients treated with cortisone, an abnormal substance which demonstrated the same ultraviolet absorption properties as that found in the Kimmelstiel-Wilson lesion. Furthermore, nondiabetic patients receiving intensive steroid therapy have developed retinal capillary aneurysms which can be demonstrated by ophthalmoscopic and histologic examination.

Although it has provided a useful stimulus to research, nevertheless the adrenocortical hypothesis remains tentative and unproved. Most discouraging has been the failure to reproduce consistent retinal lesions in experimental animals even in the presence of advanced renal glomerular lesions. At the present time, this reviewer can only echo and reemphasize the warning note of caution expressed by Rosen that "the therapeutic implications to be drawn from this approach are very tenuous if they exist at all."

BERNARD BECKER

Uveitis

PHACOGENIC UVEITIS

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Ophthalmologica, 1957, *133:* 326–329

The term of phacogenic (or phacotoxic, phacoanaphylactic) uveitis is old. Recently H. Müller published a paper on the symptomatology and morphology of this disease. The author agrees with his statements and favors the differentiation between genuine phacogenic uveitis and the phacotoxic reaction of an eye in hypermature cataract in which apparently the extensively decomposed proteins of the lens become toxins and cause phenomena of irritation. Genuine uveitis follows a severe course and is characterized particularly by a highly acute exudative and cellular reaction. In most of the cases there is no hypermature cataract present, and the complete opacification of the lens occurs only in the course of the inflammation. Three illustrative cases are presented.

The author's study is not limited to the symptomatology and morphology of the phacogenic uveitis. An attempt has been made to prove the phacogenic causation of the inflammation by the direct demonstration of autoantibodies against the proteins of the lens. Previous clinical and experimental work revealed that antibodies against various antigens may be formed in the eye. If the antigen has its seat in the eye itself, as in the case of phacogenic inflammation, there must be considerable concentration of antibody in the aqueous humor of the eye. Hemagglutination was used for this purpose.

METHOD

The anterior chamber was punctured before the performance of the operation for cataract. The cataractous lens was pulverized with isotonic sodium chloride solution and the obtained suspension (during 10 minutes with 3000 rotations per minute) was centrifuged. The overlying solution of proteins of the lens was diluted to an approximate total protein content of 1:1000. With this antigen solution the erythrocytes of a wether were sensitized according to Boyden's technic. As a stabilizing diluent a 1:1000 bovine serum albumin solution was used. The dilution series of serum and aqueous humor were placed in Kahn tubes. Readings were made after ½-hour incubation at 37°C. and 24-hour storage in the refrigerator.

The first case described was that of a 73-year-old woman with moderate irritation of the iris, a senile cataract with nuclear sclerosis and posterior opacity of the right eye, and with senile cataract of the left eye without signs of iritis. There was leukocytosis and increased sedimentation rate, but no other signs of a general disease. The inflammation became more and more acute despite antiphlogistic

and antibiotic therapy. White, crumby precipitates were observed at the posterior surface of the cornea. The lens showed rapidly increasing opacities and pronounced swelling. Considerable amounts of autoantibody against the lens were unequivocally demonstrated in the aqueous humor of this eye, with a hemagglutination titer of 1:1260, as compared with 1:160 in the serum. The phacogenic nature of this severe uveitis thus was confirmed. Cataract operation proved to be the method of choice.

The second case was that of a 50-year-old woman. A glass fragment had perforated the cornea, iris, and the anterior surface of the lens and was removed from the anterior chamber. Pressure increased, resulting in swelling of the lens, and crumby precipitates were observed at the posterior surface of the cornea. The lens was removed by linear extraction. Irritation of the eye continued for some time but subsided after treatment with prednisone. A large amount of autoantibody against the lens was found; a titer of 1:160 was observed in the aqueous humor of the eye, but the agglutination result in the serum was doubtful.

The third case was that of a 71-year-old man with a chronic granulating uveitis of both eyes which already had caused blindness in the right eye. The most probable cause was bronchiectasis and a pansinusitis. A new acute inflammation occurred and the visual acuity was reduced as the result of a rapidly developing cataract. Simultaneously the white precipitates, which were mentioned in the two previous case reports, occurred causing suspicion of a phacogenic complication. Irritation slowly subsided as a result of intracapsular surgical intervention. Autoantibodies were demonstrated in the aqueous humor of the eye with a titer of 1:160, while no definite agglutination could be demonstrated in the serum.

CONCLUSIONS

From these three case reports the clinical aspect may be outlined as follows: Phacogenic uveitis is an inflammation which is accompanied by rapidly occurring opacities of the lens. White, crumby precipitates are characteristic. Secondary glaucoma occurs almost regularly. The treatment of choice is the cataract operation. The causation of the phacogenic uveitis is still not clear. One may assume that an endogenous or, as in Case 2, an exogenous infection induced a chronic state of irritation in the eye and the lens which already had turned cataractous and became antigenic (adjuvant effect of the state of irritation). Apparently there may also be added an increased permeability of the capsule of the lens. It does not seem probable that the cataractous lens should be the only causative factor of this form of uveitis, or its incidence would be much greater. Despite that, the cataract operation exerts a favorable effect.

It is possible that one might find a phacogenic component in an additional number of patients with uveitis if one would search for it. One should not be too reluctant to perform an operation on patients with chronic uveitis complicated by cataract, particularly since today with the aid of steroid hormones and antibiotics, one is able to prevent, to a great extent, a new inflammatory bout postoperatively.

Comment: Application of immunologic technics to the aqueous humor in disease states offers hope of establishing the specificity of etiologic agents to which a presumptive role has hitherto been assigned. Precipitins against toxoplasma antigens have been demonstrated in the aqueous humor of uveitis patients by O'Connor and co-workers. The present report appears to provide evidence of autosensitization to lens protein. Woods and Burky (1934) were able to sensitize the skin to lens protein by using staphylococcal toxin as an adjuvant, but it is not necessary to assume that bacterial infection plays a part in phacogenic uveitis. In connection with the three cases reported, it would be interesting to know whether there was any cross reaction between the lens antigens and the aqueous antibodies of the three patients, and whether antibodies were present against normal and cataractous lenses of patients not showing signs of uveitis.

HENRY F. ALLEN

Miscellany

This section will be devoted to questions and answers, brief abstracts, comments and the like. Each letter must contain the writer's name and address, but these will be omitted on request.

EXOPHTHALMOS WITH CONJUNCTIVAL EDEMA

TO THE EDITOR:

What is the recent treatment for exophthalmos and conjunctival edema associated with toxic diffuse goiter (Graves' disease)?

Answer: The common type of exophthalmos associated with toxic diffuse goiter is that which parallels the course of the hyperthyroidism. This is a benign form of exophthalmos which requires no special treatment other than correction of the hyperthyroidism. Exophthalmos that is accompanied by conjunctival edema, chemosis, and extraocular muscle palsy is more likely to be the progressive or malignant type. Wide variations in the course of the exophthalmos make it almost impossible to predict the eventual outcome in any particular case. Furthermore, the unpredictable course makes it extremely difficult to determine whether improvement in the exophthalmos is due to a spontaneous remission or to the therapy that happens to be in use at the time.

In general, there is no effective medical treatment for progressive exophthalmos. If hyperthyroidism is present, it should be corrected in a positive manner by subtotal thyroidectomy after preparation with antithyroid drugs or with radioiodine (I^{131}) if the patient is over 50 years of age. There is no conclusive evidence that progression of the exophthalmos is accelerated by the elimination of hyperthyroidism. It is true that exophthalmos may progress after correction of hyperthyroidism with antithyroid drugs, with thyroidectomy, or with I^{131}, but it is also true that exophthalmos has progressed severely in the presence of active hyperthyroidism. Elimination of hyperthyroidism is, therefore, the first step in the treatment of exophthalmos.

Care of the protruding eyes should include evaluation of the head of the bed at night, protection of the cornea during the day by the use of glasses, warm compresses to the eyes three or four times a day, application of protective ointments at bedtime to avoid drying of the cornea, prompt, energetic treatment of conjunctival infection, and avoidance of excessive fatigue, excitment, or nervous tension. These measures are simply protective and do not alter the course of the exophthalmos. Treatment of exophthalmos with desiccated thyroid, triiodothyronine, cortisone, estrogens, pituitary, or orbital radiation has given such inconsistent results as to cast serious doubt on their value. If the course of the exophthalmos is steadily progressive and the degree of proptosis is such as to

jeopardize the eyes, orbital decompression by surgery is indicated without delay.

Answer: The bulk of accumulated evidence points to toxic diffuse goiter as being a thyrohypophysial syndrome, and there is much evidence to indicate that the pituitary gland is intimately connected with exophthalmos in this condition, although it is frequently dissociated from the size of the goiter or the degree of thyroid activity measurable.

Exophthalmos may appear before the occurrence of hyperthyroidism or in instances in which it is never detected. It frequently comes during increasing hyperthyroidism and not infrequently appears after its disappearance. It is thought to be due to hyperpituitarism associated with an excess output of thyroid stimulating hormone or a closely connected factor, an exophthalmos producing substance.

The types of treatment available include the following, most of which are designed to inhibit pituitary activity: It is considered good practice to correct hypothyroidism, and it is probably good practice to correct hypometabolism even though definite evidence of hypothyroidism is not present. The use of larger than physiologic doses of dessicated thyroid or triiodothyronine have been tried in the past, with only mild success, but there are now a few instances on record in which prompt and marked improvement has followed the use of large doses of triiodothyronine.

Estrogens and androgens have been used as pituitary inhibitors, but in exophthalmos they have been of little or no practical value. Some patients in this country and in England have been treated with corticotropin (ACTH), cortisone, or hydrocortisone or with combinations of these. Records to date indicate that the response to these substances is not readily practicable. Though dramatic response may occur, the improvement may in some instances be great in the actual proptosis, but in most instances, as more results accumulated, the result is chiefly on soft tissue swelling of lids and conjunctiva. In those instances in which corneal drying or beginning ulceration threatens, or the loss of an eye, orbital decompression (Nafzigger's operation) may be necessary.

The method which has recently been highly successful in a few instances was reported first in 1942; namely, the production of hypopituitarism. A similar patient has recently been reported by M. Albeaux Fernet and co-workers (J. Clin. Endocrinol.), and other unpublished data indicate that hypopituitarism caused by surgery may be followed by almost complete disappearance of all eye signs associated with severe exophthalmos.

Local eye care and local operations may be useful. One of the most important points is to prevent dryness of the cornea. This can be helped by use of protective ointments at night and the wearing of shields over the eyes to maintain a moist atmosphere over the cornea. Skin divers' goggles are useful for this purpose. If the condition is fairly marked and stationary, covering of the eye may be assisted by tarsorrhaphy. For the associated diplopia, muscle surgery has some usefulness. It has to be postponed until the condition is stationary, and its usefulness is limited because of the type of change which has occurred within the

affected muscle, rendering it relatively paralytic due to infiltration of leukocytes, mucopolysaccharides, and later with much associated fibrosis.

J. A. M. A., 1957, *164:* 1999

OCULAR EFFECTS OF ALCOHOL

TO THE EDITOR:

It has been said that diminution of the visual field is among the first manifestations of physiological disturbances caused by alcohol in drivers of motor cars. Is the fact really proved, or, on the contrary, is it scientifically denied?

Answer: The classic eye sign of alcohol intoxication is the cecocentral scotoma characteristic of tobacco-alcohol amblyopia. There is some question whether the scotoma results from alcohol alone. No available text describes constriction of the visual field as an early manifestation of physiologic disturbance caused by alcohol. Loss of visual acuity in tobacco-alcohol amblyopia is temporary and is recovered shortly after the use of tobacco is discontinued even though the use of alcohol is continued. Diminution in visual acuity occurs with optic neuritis and optic atrophy in methyl alcohol poisoning and may go into total permanent blindness. The first ocular manifestation of alcohol intoxication is diplopia and loss of judgment of distance. This disturbance is of more importance to drivers of motor cars than diminution of vision or constriction of the visual field.

Answer: It is generally assumed that the effect of alcohol on the central nervous system is due to poisoning of tissue cells so that they are unable to use oxygen properly. In other words, a state analogous to tissue anoxia is produced and would explain the striking effects of alcohol on the central nervous system, since nervous tissue is very susceptible to oxygen want. The symptoms of anoxia in relation to vision are diminished visual acuity, constriction of the visual fields, reduction in retinal sensitivity, and increased fatigability of the muscles of accommodation and convergence (Wilmer and Berens: J. A. M. A., 1918, *71:* 1394–1398). A progressive loss in the visual fields with increasing lack of oxygen has also been reported by Evans and McFarland (Am. J. Ophth., 1938, *21:* 968).

In studying the relationship of alcoholic intoxication and anoxemia, it has been shown that an excess of oxygen and carbon dioxide tended to sober up the subjects more rapidly and that they did better in psychologic tests (McFarland and Barach: Am. J. M. Sc., 1936, *192:* 182).

J. A. M. A., 1957, *164:* 2100

PSEUDO-ARGYLL ROBERTSON PUPILS WITH ABSENT TENDON REFLEXES

A Benign Disorder Simulating Tabes Dorsalis

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Brit. M. J., 1931, *1:* 928–930

I wish to draw attention to a benign symptomless disorder characterized by pupils which react on accommodation but not to light, any by absent tendon reflexes.

Five of the six cases I am about to describe came under my notice in the course of a few weeks; the condition therefore cannot be very rare. Though harmless in itself it merits recognition because it is often mistaken for a manifestation of syphilis of the nervous system, with unfortunate consequences for the patients and their families.

Case I. A woman aged 36 was admitted to the Hospital for Tropical Diseases under the care of Dr. G. Carmichael Low for an "overhaul" on her return from abroad. Physical examination and routine laboratory tests revealed no evidence of disease apart from the neurologic signs that concern us here. There was nothing in the family or personal history to explain these signs. Ten years ago she noticed that her pupils were unequal. On examination I found pupils of moderate size, the right just larger than the left, which was slightly oval; neither reacted to light, direct or consensual; both contracted fully on convergence, but the movement was remarkably slow; after the effort to converge was relaxed they remained small for several seconds, then dilated very gradually to their original size. All the tendon reflexes in the upper and lower limbs were completely abolished. There were no other signs of organic nervous disease. I knew that this myotonic pupillary reaction had nothing to do with syphilis, but had never seen or heard of it in association with absent tendon reflexes. I reported as follows: "A most unusual case; I prefer not to make a diagnosis; the condition is benign, and should not prevent her from returning to her work abroad." After her discharge, Dr. Low kindly allowed me to consult the hospital notes, and I found that Wassermann's test had been done on the blood and cerebrospinal fluid with negative results.

Case II. A woman aged 23 attended hospital because her brother, an optician, had found that she had Argyll Robertson pupils. She was admitted to the National Hospital for investigation. She knew "what they thought," and was greatly

WILLIAM JOHN ADIE

(1886–1935)

distressed. With the first case in mind I promised her that she should leave the hospital with the stigma removed. Apart from the special signs, nothing of importance was discovered in the course of a thorough routine investigation. The following observations were made: the pupils were unequal, right 3½ mm.,

left 3 mm.; the right was irregularly oval with the long axis vertical, the left regularly oval with the long axis horizontal. The reaction to light was completely absent in both; the reaction on convergence was present in both, but was abnormal; the contraction was delayed and proceeded slowly until the pupils reached pinpoint size. When the effort to converge was relaxed they dilated very slowly to their original size. The knee and ankle jerks were completely absent. These observations were confirmed repeatedly by myself and my colleagues. The Wassermann reaction was negative in the blood and cerebrospinal fluid. The report on the fluid was as follows: clear, colorless; no cells seen; total protein 0.035 per cent; Nonne-Apelt and Pandy reactions negative; Lange's colloidal gold test, no change (Dr. J. G. Greenfield).

Case III. A young man now aged 32 was brought to me 12 years ago by his sister, a medical student, who discovered that he had Argyll Robertson pupils. I found that his knee jerks were absent, and thought that he was a case of congenital tabes. He came to see me recently about another matter, and I went into his family and personal history and made a complete physical examination. Nothing apart from the neurologic signs suggested syphilis, congenital or acquired. His general health was good. The pupils were moderate in size and unequal, right larger than left. The right was totally inactive to light, the left reacted very feebly. On convergence both pupils contracted very slowly to pinhead size, then dilated still more slowly when he looked into the distance. He had noticed himself that the pupils varied in size from time to time. All the tendon reflexes in the upper and lower limbs were absent. There were no other neurologic signs. He has submitted to several tests of the blood and cerebrospinal fluid, all with negative results.

Case IV. A woman aged 45 attended the Royal London Ophthalmic Hospital for glasses and was referred to me by Mr. Foster Moore, who had noticed the abnormal pupils. There was nothing worthy of note in the family or personal history. Her general physical condition was good. Vision improved to 6/9 right, 6/18 left; no optic atrophy (Mr. Foster Moore). The pupils were unequal; right 3 mm., left 2½ mm. The left pupil did not react to light; on convergence it contracted slowly but fully, and maintained its smaller size long after convergence had ceased; it then dilated very gradually. The right pupil contracted feebly to light, slightly better on convergence; the contraction was not slow or unduly maintained. The knee jerks were easily obtained and equal, but the ankle jerks were completely absent. The Wassermann reaction in the blood was negative. The cerobrospinal fluid has not yet been examined.

Case V. A girl aged 17 was referred to me by Mr. Foster Moore and admitted to the National Hospital for investigation. She noticed about two years ago that her pupils were unequal, and that the left pupil varied in size from time to time. Four months ago the left pupil became permanently large; since then she has not been able to use it for close work. Otherwise she has always been in perfect health. Examination revealed no other signs except the following: The pupils were unequal; right 2½ mm., left 8 mm. They were both inactive to light; on convergence the right pupil contracted slowly to pinpoint size, and when con-

vergence ceased it again dilated very slowly. The left did not contract on convergence. The knee jerks were brisk. For a patient of her age and compared with the active knee jerks, the ankle jerks were certainly abnormally sluggish. The Wassermann reaction was negative in the blood and cerebrospinal fluid. Report on the cerebrospinal fluid: clear, colorless, 1 cell per c. mm.; total protein 0.03 per cent.; Nonne-Apelt and Pandy reactions negative; Lange's colloidal gold reaction 0001100000 (Dr. J. G. Greenfield).

Case VI. In an article on the myotonic pupil in Wilbrand and Saenger's Neurologie des Auges, I found a reference to a case described by Gehrcke in which eye signs like those in my cases were found in a patient with "imperfect stationary tabes." The following is an extract of the case history: A woman aged 45; right pupil inactive to light, very slow contraction and relaxation on convergence; ankle jerks absent. There were no other signs of organic nervous disease. The family history was not given. The Wassermann reaction was negative in the blood and cerebrospinal fluid. The Nonne-Apelt, Weichbrodt, and Pandy reactions were all negative; no increase of cells; pressure normal. Nevertheless, because the ankle jerks were absent the diagnosis of tabes was made. This is the only case resembling my own that I have been able to find in the literature. I have not yet completed my search. (See note at end.)

COMMENTARY

It is not surprising that all of these patients with "Argyll Robertson pupils" and absent tendon reflexes were thought to be suffering from syphilis of the nervous system, congenital or acquired. The correct diagnosis can be made with certainty by closely observing the contraction of the pupil during the act of accommodation for near objects. The true Argyll Robertson pupil reacts promptly and fully, often excessively, on convergence, and dilates again as soon as the effort to converge the visual axes is relaxed. In these cases the pupils show the so-called myotonic reaction; they do not respond to light; they contract very slowly through a wide range during a sustained effort to converge; often remain small long after the efforts ends, and, when they dilate again, do so slowly. They differ in other ways from the true Argyll Robertson pupil, but the above features are sufficient to distinguish them. This myotonic reaction is well known to ophthalmologists, and it has been firmly established that syphilis plays no part in its production. Mr. Foster Moore has described seven cases under the title "nonluetic Argyll Robertson pupil," and has told me of several others he has seen. The characteristics of his cases are, he says, the complete or substantially complete inaction of the pupil to the light stimulus, the leisurely manner in which it contracts with convergence, and in which it again dilates after relaxation of convergence; the frequency with which it is unilateral; the integrity of accommodation; the absence of syphilis; the presence of knee jerks, and the absence of signs of any nervous disease even after many years.

It seems to me more than probable that some of his cases with nonluetic Argyll Robertson pupils but normal tendon reflexes are examples of a milder form of the same benign disorder that I have described here. I think, too, that my cases are

related to those described by Mr. Gayer Morgan and Dr. C. P. Symonds under the titles "A series of cases with rapid onset of unequal pupils and failure of accommodation: a *forme fruste* of encephalitis lethargica," and "Internal ophthalmoplegia with absent tendon reflexes." In their cases the defect was most often unilateral, the affected pupil was dilated, and reacted not at all or incompletely both to light and on convergence; further, accommodation was partially paralyzed, so that visual symptoms were produced. In some of their cases the tendon reflexes were diminished or lost.

My fifth patient seems to me to provide evidence that links the three groups. In one eye her pupil was dilated and fixed, with paralysis of accommodation, as in the cases described by Mr. Morgan and Dr. Symonds; in the other eye accommodation was normal, the light reflex was absent, and the reaction on convergence was myotonic as in the nonluetic Argyll Robertson pupils of Mr. Foster Moore. My fourth case also showed a myotonic pupil on one side and a partially fixed pupil on the other. I have reason to believe that a large fixed pupil is sometimes the forerunner of a myotonic pupil. These and other more academic aspects of the subject I hope to deal with at another time. My object now is to make it known that pupils conforming to the prevailing loose definition of an Argyll Robertson pupil, and easily mistaken for the true Argyll Robertson sign, may be found associated with loss of tendon reflexes in patients with a benign disorder that has nothing to do with syphilis whatsoever.

Note. After this was written, Mr. Foster Moore kindly allowed me to read the typescript of his paper on the nonluetic Argyll Robertson pupil, which he read at the recent Ophthalmological Congress. In one of his 15 patients with this abnormal reaction of the pupil, the knee jerks were absent; in another they were obtained with reinforcement only.

Editorial comment: The myotonic pupillary reaction had been previously described independently by Saenger and Strasburger in 1902. Nonne then observed the association with absent knee and ankle jerks. Adie's first paper on the subject in the British Medical Journal was followed by two additional contributions the following year (Brain, 1932, *55:* 98; Brit. J. Ophth., 1932, *16:* 449) in which he emphasized the atypical forms of the malady and its widespread incidence. The importance of the Adie syndrome, which is essentially benign, rests chiefly in its differential diagnosis from the Argyll Robertson pupil and tabes. The Adie pupil occurs predominantly in females, and is unilateral in 80 per cent of cases. The affected pupil is relatively dilated and its response to a light stimulus (either direct or consensual) and to convergence is so excessively slow as hardly to be noticeable except after dark adaptation, though the fellow pupil reacts normally. The condition is most common in the third decade, is noted suddenly and is permanent. The reactions to atropine, homatropine, cocaine, epinephrine, eserine and pilocarpine are normal though a relative difference in the size of the pupils continues. In contradistinction the Argyll Robertson pupil affects males predominantly, and is bilateral in 90 per cent of cases; the pupils react readily to convergence and mydriatics produce a slow, incomplete response. Scheie noted that while the instillation of methacholine chloride (mecholyl) in 2.5 per cent concentration does not affect the normal pupil, it produces a prompt constriction of the myotonic pupil. This diagnostic test would seem to place the site of the lesion at the ciliary ganglion or postganglionic fibers. In support of this view

Weekers reported four cases in which the retrobulbar injection of ethyl alcohol caused a permanent myotonic pupil, which constricted promptly to stable derivatives of acetylcholine such as mecholyl but not to cholinesterase inhibitors (eserine, isoflurophosphate). Much clinical evidence, however, suggests also an involvement of the diencephalon and its connections.

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BIOGRAPHICAL NOTE

William John Adie (1886–1935) was born in Geelong, Australia, and qualified in medicine at Edinburgh University. In World War I he was cited for gallantry in the field and during the initial gas attacks improvised a urine-dampened mask. After the war he rejoined the neurologic staff of the National Hospital and was appointed physician to the Royal London Ophthalmic Hospital. While at the latter institution Adie wrote on the syndrome of tonic pupils and absent tendon and periosteal reflexes. He was the first to describe the syndrome in detail and to delineate complete and incomplete forms. His other principal contributions were on dystrophia myotonica and narcolepsy. His clinical acumen and teaching ability were noteworthy. In his last years while convalescing from coronary thrombosis at Majorca, he became increasingly engrossed in his hobby of ornithology and bird watching.

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JELLIFFE, S. E.: Obituary. J. Nerv. & Ment. Dis., 1935, *81:* 726.

Book Reviews

"Clinical Neuro-Ophthalmology," by Frank Walsh (*The Williams & Wilkins Co., Baltimore, 1956, 1294 pp., 441 illustrations, $29.00*) *is the second addition of an ophthalmic classic. It is reviewed here by John W. Henderson of the University of Michigan.*

The publication of the second edition of this excellent book has been impatiently awaited by many of us, and the result is well worth the waiting. The magnitude of the material covered and the thoroughness of the discussions makes a difficult task for the reviewer—somewhat akin to a review of the Good Book where every word seems important.

Since the appearance of the first edition the widespread acceptance of Walsh's *Clinical Neuro-Ophthalmology* has extended well beyond the field of ophthalmology. My neurosurgical colleagues feel that this is one of their best texts as well, and ready acceptance has been gained from neurologists.

The second edition holds worthwhile improvements. The table of contents is more complete, and the index has been thoroughly revised in a more useful form. The three column format is easier to read, and the style remains of a clarity which we all have come to expect from the author. The reproduction of the illustrations is of better quality than in the first edition, and over 100 new case summaries have been added. The use of bold face print in the subtitles rather than italics makes for easier search for material.

Dr. Walsh states in his preface that important new material has been included, and perusal of the two editions side by side reveals the scope of such additions. The discussion of the blood supply to the visual pathway has been consolidated and includes the recent work of Francois and Neetens on the supply of the optic nerve. The inclusion of the extinction phenomenon in visual field testing brings us up to date, although perhaps a further discussion of flicker fusion fields would be indicated. The topical diagnosis of third nerve lesions has been expanded to include a valuable new illustration as well as a thorough discussion of Jefferson's latest work on cavernous sinus involvement. Recent information on recurrent facial nerve palsy and on section of the greater superficial petrosal nerve for bullous keratitis has been added.

In discussing clinical tests for sympathetic paralysis, Walsh notes the lack of reliability of the use of cocaine and of Adrenalin as judged by pupillary response rather than giving the classical findings which were noted in the first edition. Material on the new syndrome of central autonomic dysfunction with defective lacrimation has been added. Discussion of stellate ganglion block for central arterial occlusion is included. Recent evidence of active sympathetic stimulation rather than parasympathetic inhibition in pupillary dilation is cited.

The author has lost his enthusiasm over alcohol injection of the orbicularis for essential blepharospasm, and feels that psychotherapy is often indicated.

One case of aberrant regeneration of the oculomotor nerve as the result of brain tumor has been added; usually such a finding rules out intracranial tumor.

It is interesting to read the expanded section on proprioception and the extraocular muscles. Recent evidence of muscle spindles present in these muscles is given, as well as reference to Ludvigh's recent work. This is interesting to the reviewer who has always been annoyed at the assumption that active proprioception must be conscious in order to exist, when it is well known that not all proprioceptive sense elsewhere reaches consciousness. The section on strabismus has been greatly expanded. Recent advances in the knowledge of supranuclear and other controlling mechanisms for ocular movement have been duly noted, notably Cogan's work on cerebellar relationships to ocular movement and his discussion on ocular apraxia.

The new edition reviews the work of Carroll, and of Taub and Rucker on the etiology of optic neuritis. Although the work of the Academy Symposium of 1955 is quoted as showing no specific advantages of corticosteroid therapy over more conventional means in optic neuritis, it is interesting to the reviewer that Walsh uses Meticorten for those cases with disk swelling, as opposed to vitamin B_{12} and time for those without disk changes.

Hyaline bodies of the optic disks are discussed in detail, with exposition of the associated visual field defects. The rewritten section on retrolental fibroplasia will be most helpful for our neurologic associates who will use this book. The expansion of both the text and the bibliography in the section on congenital abnormalities certainly reflects an awakening interest in this field by many writers. It would have been helpful to include the recent work on the surgical treatment of hydrocephalus in this section, such as the Matson procedure of subarachnoid renal shunt

In the section on infections, the important work of Murray and Walsh on the ocular signs of poliomyelitis has been added. Choked disks may occur in the convalescent stage of the disease and may be dependent upon increased spinal fluid protein levels; optic neuritis is unlikely; the usual peripheral palsy encountered is that of the abducens; and there is rarely any permanent ocular disability. The mucocutaneous syndromes have been added. Case histories and visual field diagrams have been included to expand the section on opticochiasmatic arachnoiditis. The changing outlook in the ocular findings in tuberculous meningitis is duly noted, now that recovery is possible with drug therapy. The section on mucormycosis is a newcomer. It is exciting to note the addition of specific therapy for many of the diseases—notably those due to rickettsia—between the two editions. Increased knowledge of toxoplasmosis is reflected both in the text and the bibliography. The treatment of central nervous system syphilis has been brought up to date, stressing the value of penicillin.

Recent work on the relationship of altered copper metabolism in Wilson's disease and the use of British anti-Lewisite (BAL) to mobilize copper in this condition are included. The ferment of varying ideas with regard to progressive exophthalmos of thyroid disease is reflected in the expanded section. Treatment is covered in detail, including the evaluation of irradiation to the pituitary vs.

the orbit. Not mentioned is the possibility of hypothalamic change from the same treatment, a fact documented in monkeys. Papilledema and optic neuritis in hypoparathyroidism are discussed. Recent work on hypophysectomy for diabetic retinopathy in juvenile diabetes is noted, although only one case had been so treated at the Johns Hopkins Hospital at the time of writing. Among the new disease entities added to this section are Letterer-Siwe's disease, galactosemia, and amyloidosis.

In the chapter on disorders of muscles, newer work in myasthenia gravis has been included—the use of Tensilon in diagnosis, and newer drugs in treatment, such as tetraethyl pyrophosphate (TEPP). An interesting case of exophthalmos which decreased on Prostigmine administration is added, with photographs. A short summary by Breinin on the current status of electromyography as a diagnostic tool in neuroophthalmology is included.

Considerable work on thrombosis of the carotid artery has appeared since the first edition. This is brought up to date admirably, and the ocular signs mentioned have included homonymous hemianopsia, pupillary changes, and more rarely a homolateral optic atrophy. Where homonymous hemianopsia occurs, relative sparing of the upper half fields is related to the blood supply of the lower visual radiations by way of the posterior cerebral artery. The recent work of Sachs demonstrating collateral circulation to the ophthalmic from the external carotid artery by arteriography has been added. The evidence gained by anterior choroidal artery ligation for Parkinson's disease shows that visual field loss does not follow in most instances. An excellent new section on arteriography has been added, with notable roentgenographic reproductions. The discussion on intracranial aneurysms represents a monograph in itself, and has been brought up to date. This remains one of the outstanding sections of the book and has been aided by several new figures.

In discussing the bruit present in carotid cavernous fistula the author notes that vascular anomalies in the orbit may produce a bruit, as well as some cases of increased intracranial pressure, where it may be due to kinking of major vessels. The author's work (with Hedges) on optic nerve sheath hemorrhage has been included in the section on subarachnoid hemorrhage. Informative tables from Cannon's paper have been added to indicate the primary pathology, symptoms and signs of acute vascular lesions of the brain stem. The addition of pulseless disease with related ocular findings reflects the recent interest in this subject. No mention is made of steroid treatment in periarteritis nodosa, and it would be helpful if temporal arteritis were discussed along with this diesase. In expanding the discussion of cardiac malformations and their surgical treatment, pulmonary arteriovenous fistula, hereditary methemoglobinemic cyanosis, and coarctation of the aorta are new. An entirely new discussion of infectious mononucleosis and its ocular signs has been added.

Posterior orbital encephalocele as a result of neurofibromatosis to produce pulsating exophthalmos is considered the next in frequency after carotid cavernous fistula. Interesting new photographs are included in the discussion of Sturge-Weber's disease. Lethal midline granuloma has also appeared since the

first edition. New illustrations and text material on nasopharyngeal tumors have been added, giving details of the related cranial nerve involvement. The excellent section on pituitary tumors has been enlarged to include several new illustrations and added discussion.

The chapter on injuries includes many new illustrative case histories. There is addition of leptomeningeal cysts as the result of head trauma. The involvement of the optic nerve in injuries has been expanded in the text. Traumatic encephalocele of the orbit is discussed, including an excellent photograph. The ocular complications of cerebral angiography are reviewed. Mention is made of the higher incidence of hemorrhages of the conjunctiva and retina noted by Falls, Bassett and Lamberts. (It is likely that their figures were a reflection of the technic used in the injection of contrast mediums then in vogue, since similar findings are much less frequent in our hospital at present.—*Ed.*) Atomic bomb injuries have been added to the section on radiation results.

Photogenic epilepsy is now included in the section on convulsive disorders. Mention is made of the newer surgical procedures for trigeminal neuralgia such as that of Taarnhoj. Walsh has seen two patients with transient ocular palsies thereafter.

The chapter on the ocular signs of mental disease has been rewritten to a great extent. The final chapter on drugs, poisons and toxic amblyopias includes 27 new substances.

Indeed, this is a monumental work. It should be in the library of every ophthalmologist and specialist dealing with neurologic disease. Suffice it to say that the first edition in our clinic was literally worn out by the constant use of the residents. We all owe a great debt of gratitude to Dr. Walsh.

"Accommodation and Binocular Vision," by Dr. Robert Siebeck (*Carl Marhold Verlag, Halle, 1957, 100 pp., 54 fig., DM 26.25*) *discusses the synergistic mechanisms which facilitate depth perception particularly emphasizing unequal accommodation of the two eyes. It is reviewed here by Arthur Linksz.*

Ever since Carl Hess (one of the most outstanding German ophthalmologists of the early twentieth century) seemingly refuted contrary assertions, it has generally been taken for granted that accommodation affects both eyes equally whatever stimulus might be the effective cause of it. The author of this interesting monograph collected sufficient evidence for the reasonable assumption that, under certain conditions, accommodation in the two eyes might be unequal. He had the opportunity to study the accommodative changes *objectively*, with the help of retinoscopy, in the myopic eye of two patients with unilateral myopia while their other, near emmetropic, eye accommodated for several measured distances. He feels confident to conclude from his studies that, in near vision, the refraction of the eyes became equalized to a certain degree due to a lesser amount of accommodation in the emmetropic eye than the other.

Here then would be a mechanism which facilitates fusion, a less conspicuous intraocular mechanism besides the much better known and much more evident extraocular motor mechanism. The author feels with Colenbrander that accom-

modation is "learned" and that in the isometrope equal accommodation becomes a conditioned reflex while in the anisometrope it is the unequal accommodation which becomes conditioned. The author feels that it is this conditioned unequality of accommodation rather than the unequal magnitude of the retinal images which, in the anisometrope, often prevents comfortable binocular vision with full refractive correction. This is certainly food for further thought.

Binocular vision for near in the unilaterally myope is facilitated by a lesser accommodative effort in the myopic eye. In the unilateral hyperope this royal road is closed. He will have to exert a lesser accommodative effort for both distance and near with his emmetropic (or less hyperopic) eye, thus constantly facilitating the use of this eye and the suppression of the impressions of the other eye. In fact, unilateral amblyopia is much less common in unilateral myopia than unilateral hyperopia. In one case of unilateral hyperopia with amblyopia and strabismus, the author found a lesser amount of accommodation in the amblyopic eye than that called for by the accommodative effort of the other eye. If this is correct, then the blurring of the retinal image in the amblyopic eye is even greater in near than in far vision—certainly facilitating suppression rather than binocular vision.

The author assumes not only that accommodation is conditioned, in other words "learned," but also that it can be "unlearned." He has only one case of unilateral acquired blindness to prove his thesis, but a good one, in any event, since the blind eye was intact and blindness occurred due to an injury to the optic nerve. Accommodation in this eye was less than that commensurate with the accommodative effort in the other eye.

In unilateral strabismus with amblyopia exanopsia, accommodation of the squinting eye was found diminished even if there was little refractive difference. While the master eye accommodated for 1 m. or ½ m. the amblyopic eye hardly changed refraction. Only by accommodation at much shorter distances (20 cm. or less) is there a commensurate effect noticeable in the amblyopic eye. In alternating strabismus with equal vision in both eyes, determination of accommodation in the momentarily squinting eye was extremely difficult since the technic of the investigation (dynamic retinoscopy of the second eye while the first eye fixated a chart at variable distances) readily forced the squinting eye to take over fixation and accommodate. By the way, squinting eyes were also found poorer in relaxing for distance.

In some of the author's cases of unilateral amblyopia convergence for near was also diminished and in one case of total lack of convergence the pupillary near reaction was also missing. This might indicate that this reaction is associated with convergence rather than the accommodative effort.

Interesting as all this work is, it will need confirmation and the technic of examination needs much improvement. The problem is certainly worth restudying. We are used to thinking in terms of Hering's law of equal innervation running to terms of extraocular muscles attached to the two eyeballs. Still under certain conditions the *actual* excursion of one eye is different from that of the other (asymetric convergence in lateral version). Similarly, accommodation is at

least to become, or remain, unequal in case equal accommodation (a conditioned double reflex in the author's view) fails to realize its own reward.

Should the author's investigations turn out to be correct then (as the author correctly remarks) orthoptic treatment will have to be mindful of another obstacle to success—the possibility that squinting eyes, even if well aligned on their targets in the modern orthoptic instrument, might be unequally accommodated at their respective targets.

This review has only dealt with the last 60 pages, the *clinical part* of this 100-page monograph. It should, however, not be left unmentioned that the first 40 pages contain an excellent theoretic introduction into problems of accommodation and convergence and their possible or probable role in space perception. The beautiful studies of Fincham on the accommodative stimulus are well analyzed. The presentation of this complex topic in Siebeck's review is almost more lucid than its original description by Fincham himself.

"Slit Lamp Gonioscopy," by George Gorin and Adolph Posner (*The Williams & Wilkins Co., Baltimore, 1957, 176 pp., 67 figs., $7.00*) *is an introductory textbook intended to initiate the ophthalmologist in the principles and technics of gonioscopy and to guide him in the interpretation of his findings. It is reviewed here by H. Saul Sugar.*

As an outgrowth of their courses conducted at the Manhattan Eye, Ear and Throat Hospital, Gorin and Posner have compiled a readable and rather comprehensive handbook on gonioscopy.

The anatomy, histology and embryology of the angle are covered in the first two chapters.

A chapter on the history of gonioscopy is particularly interesting in that the priority discussion between Trantas and Salzmann is documented by the original material of Trantas and the Salzmann reply to Trantas' claim. The latter is a beautiful example of the careful, courteous and scientific approach which might be emulated whenever such a priority feud arises. The development of the various instruments and technics is described in chronologic order, both in this chapter and in one on the technic of slit lamp gonioscopy.

Five chapters cover the gonioscopic appearance of normal and glaucomatous eyes, primary, congenital and secondary. In the discussion on glaucoma, the authors state that this reviewer believes that there is no causal relationship between central retinal vein thrombosis and glaucoma simplex but that he considers both are due to a common factor, probably vascular sclerosis. As a matter of fact, it was pointed out in the original paper that the glaucoma may result directly in vascular changes leading to thrombosis but that thrombosis itself is not directly related to simple glaucoma but, rather, to a special type of secondary glaucoma associated with rubeosis. In patients with venous occlusion, usually with branch involvement, simple glaucoma which supervened was believed to be only indirectly related.

The discussion on malignant glaucoma is good. There is a chapter on gonioscopy after antiglaucoma operations, as well as chapters on congenital anoma-

lies, tumors, injuries and inflammation in the angle region. The final chapter is a discussion of gonioscopy in routine office procedure. In this chapter the authors state that in eyes with extremely narrow angles even moderate pressure on the eye during gonioscopy may be sufficient to precipitate an acute attack. It would be interesting to have such a statement substantiated by subsequent reports of any such clinical observations.

This book is a well prepared survey of the essentials of gonioscopy and is particularly well suited for today's training programs in ophthalmology.

"The Eye in General Practice," by C. R. S. Jackson (*The Williams & Wilkins Co., Baltimore, 1957, 152 pp., 25 figs., $5.00*) *is a useful introduction to ophthalmology. The review from the Journal of the American Medical Association is reprinted here.*

This little volume, a condensed version of a classic textbook on ophthalmology of 10 years ago, was compiled "with the special needs of the general practitioner in mind," and it also is just what is needed for nurses, school teachers, optometrists, opticians, and parents, for it gives in clear language the pertinent facts about the eye and its disorders. Anatomy, physiology, and mathematical optics are barely touched on and then only in terms familiar to lay persons. Only the most common of eye diseases are mentioned. There is no mention of "indications for surgery" nor directions for treatment of any disorder. The chapter on diseases of the eye is short but excellent for first aid attendants, school physicians, and country doctors who must be able to care for the simple disorders and leave the complicated cases to the specialist with modern hospital facilities. A short chapter on the eye in diseases of other parts discusses briefly but comprehensively the role of the eye in diseases of the cardiovascular system and in intracranial, endocrine, and metabolic disorders and other conditions. The last chapter deals with administrative problems of the local British Public Service to the visually handicapped. The book is the answer to the inquiry of the high school student who writes, "Please send me all information about the eyes as I'm writing a paper."

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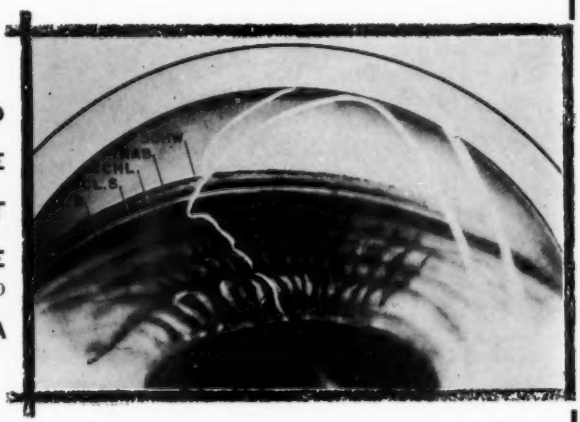

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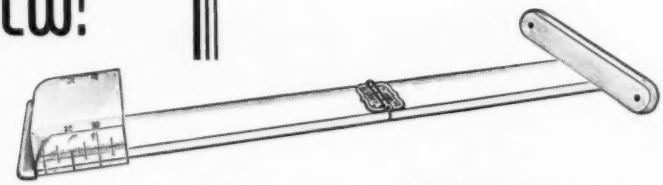

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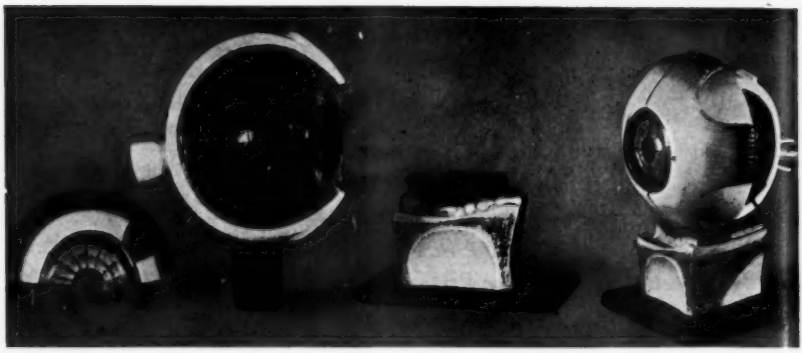

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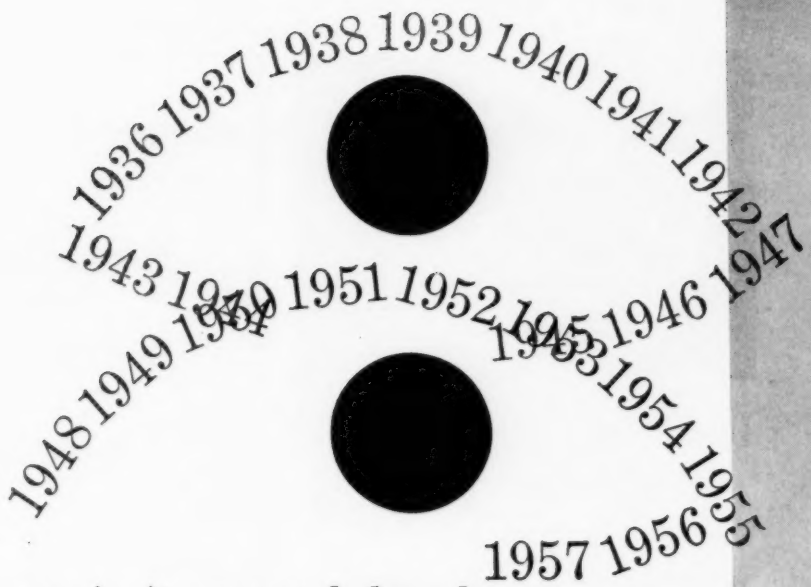

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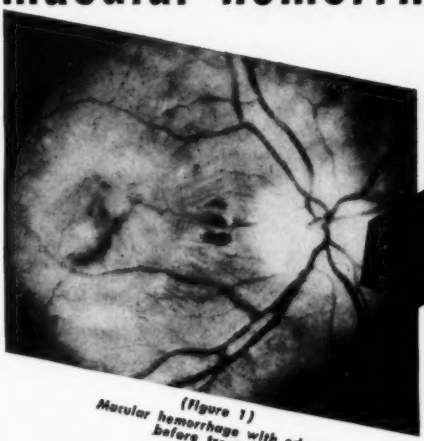
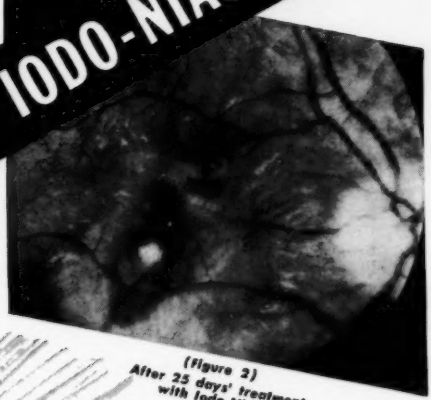


(Figure 1)
Macular hemorrhage with edema, before treatment



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2. *Am. J. Digest Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.
4. *Cecil's Textbook of Medicine*, 7th ed., 1947, p. 1598.

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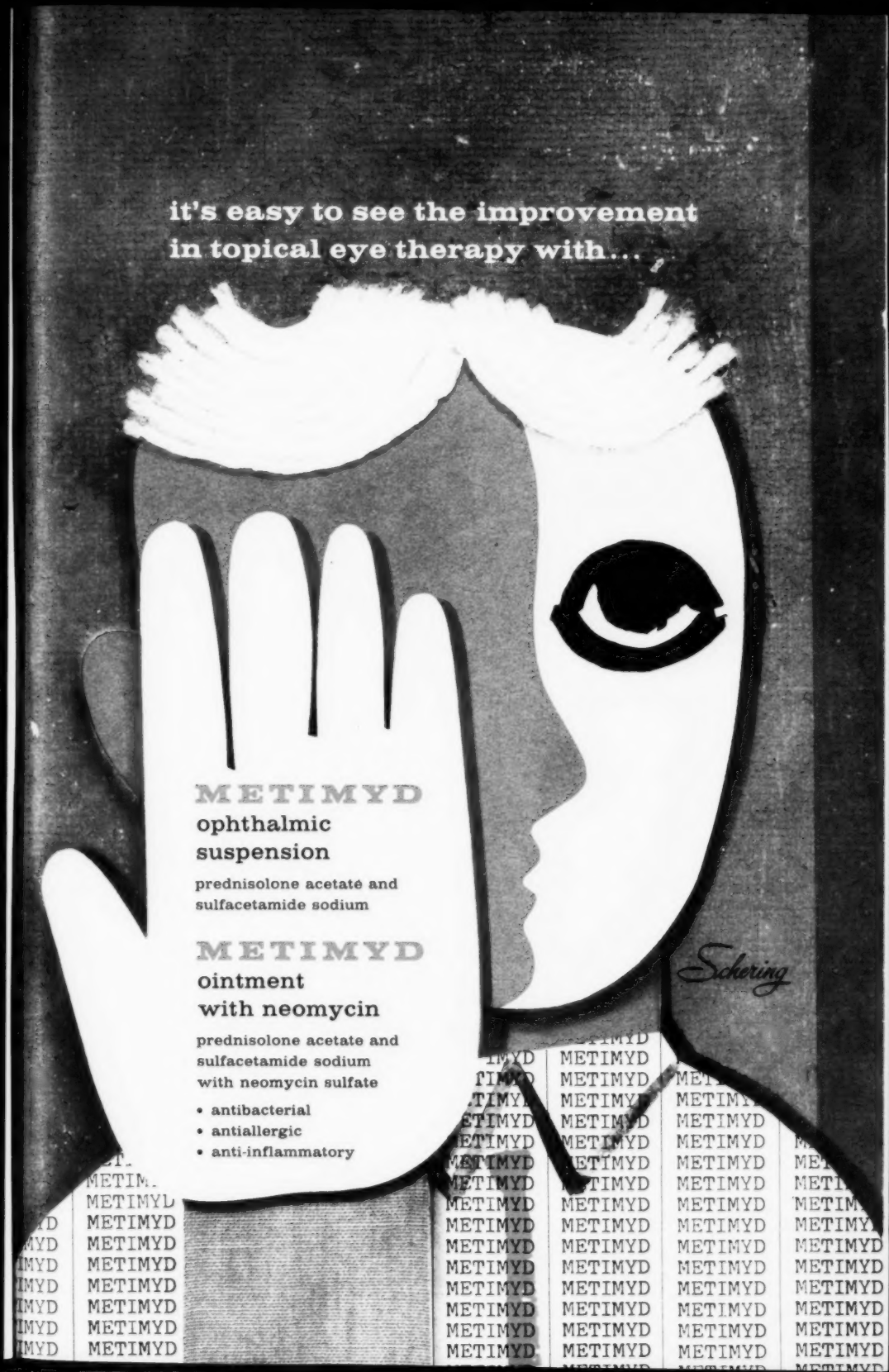
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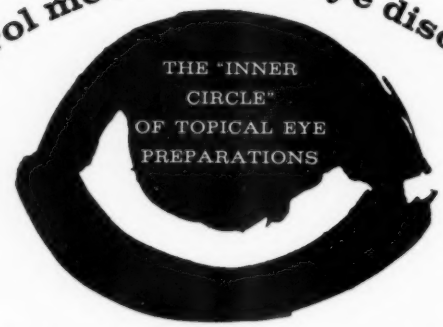

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